09/730,929

C-A-S- 11/6/02

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L4 ANSWER 1 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:778718 CAPLUS
TITLE: Methods and compositions for enhancing pharmaceutical treatments
INVENTOR(S): Newman, Michael J.; Dixon, William Ross
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 684,293.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002147197	A1	20021010	US 2002-104549	20020320
PRIORITY APPLN. INFO.:			US 1999-158322P P	19991008
			US 2000-684293 A2	20001006

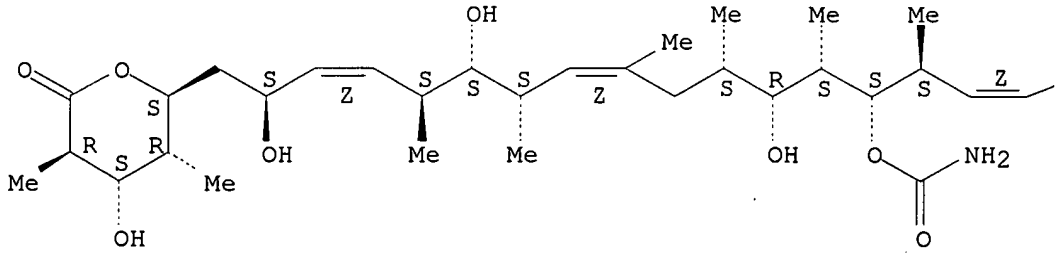
AB Improved methods are provided for therapeutic and/or preventative treatment to a mammal in which the mammal is protected against the toxicity of active pharmaceutical agents that (i) bind to or are substrates for P-gp, (ii) are taxane analogs, and/or (iii) are inhibitors of tubulin disassembly. Addnl. provided are compns. and methods useful for treating cell proliferative disorders. Further provided are methods of increasing the bioavailability of therapeutic and/or preventative treatments in a mammal. Particular embodiments are directed to increasing such bioavailability across the blood-brain barrier.

IT **127943-53-7**, Discodermolide **127943-53-7D**,
Discodermolide, derivs., analogs, and metabolites
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing pharmaceutical treatments)

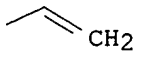
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



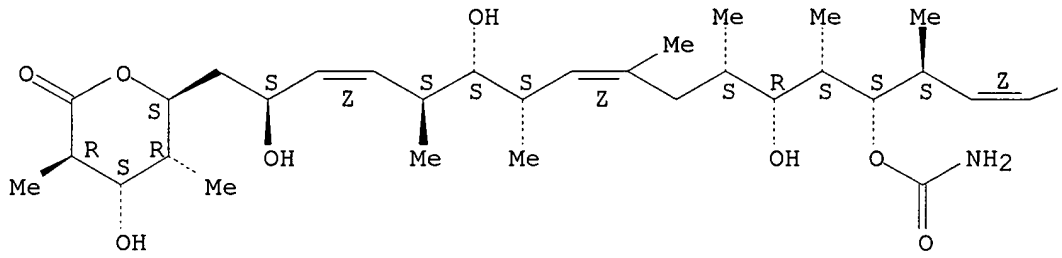
PAGE 1-B



RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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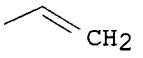


L4 ANSWER 2 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:716079 CAPLUS
DOCUMENT NUMBER: 137:242152
TITLE: Combination of epothilone analogs and chemotherapeutic agents for the treatment of proliferative diseases
INVENTOR(S): Lee, Francis Y. F.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072085	A1	20020919	WO 2002-US6746	20020305

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-275801P P 20010314
US 2001-316395P P 20010831

OTHER SOURCE(S): MARPAT 137:242152

AB The invention discloses use of a combination of epothilone analogs and antitumor agents for the treatment and prevention of proliferative disorders.

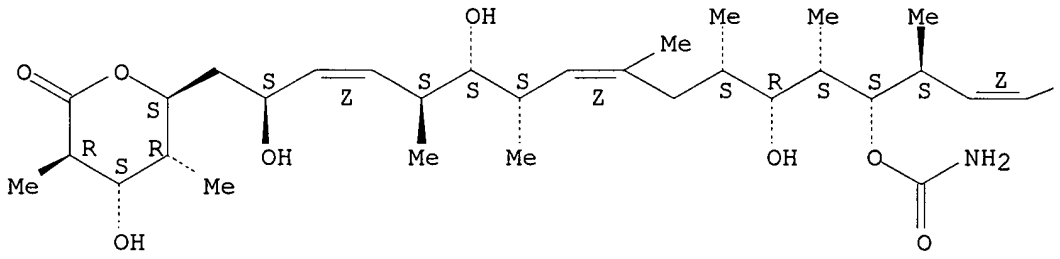
IT **127943-53-7**, Discodermolide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of epothilone analogs and antitumor agents for treatment of proliferative diseases)

RN 127943-53-7 CAPLUS

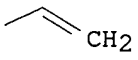
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:615354 CAPLUS
DOCUMENT NUMBER: 137:150276
TITLE: Coumarin compounds as microtubule stabilizing agents, and therapeutic uses thereof
INVENTOR(S): Jacobs, Robert S.; Wilson, Leslie; Madari, Hamta
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062293	A2	20020815	WO 2002-US2737	20020201
WO 2002062293	A3	20021003		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002151560	A1	20021017	US 2002-60317	20020201

PRIORITY APPLN. INFO.: US 2001-265576P P 20010202
US 2001-283366P P 20010413

AB Compds. and compns. for stabilizing microtubules are disclosed. Also disclosed are methods of inhibiting, preventing, regulating, modulating, attenuating, stabilizing, or affecting microtubule formation or function. Methods of treating, preventing or inhibiting diseases and disorders assocd. with microtubule formation, function, or both by administering a microtubule stabilizing agent such as coumarin is also disclosed.

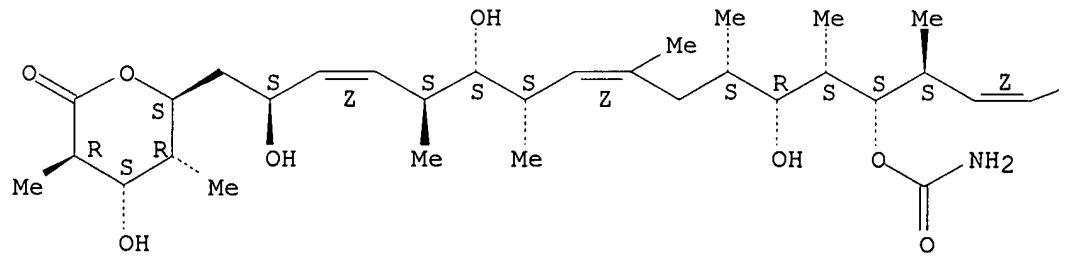
IT **127943-53-7**, Discodermolide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coumarin compds. as microtubule stabilizing agents, and therapeutic uses)

RN 127943-53-7 CAPLUS

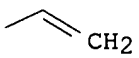
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 4 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:575783 CAPLUS
DOCUMENT NUMBER: 137:125048
TITLE: Preparation of compounds which mimic the chemical and biological properties of discodermolide
INVENTOR(S): Smith, Amos B.; Beauchamp, Thomas J.; Lamarche, Matthew J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 127 pp., Cont.-in-part of U. S. Ser. No. 455,649.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002103387	A1	20020801	US 2000-730929	20001206
US 5789605	A	19980804	US 1996-759817	19961203
US 6031133	A	20000229	US 1998-21878	19980211
US 6242616	B1	20010605	US 1999-455649	19991207
WO 2002046150	A2	20020613	WO 2001-US47958	20011206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:
US 1996-759817 A2 19961203
US 1998-21878 A2 19980211
US 1999-455649 A2 19991207
US 1998-121551 A2 19980723
US 2000-730929 A 20001206

OTHER SOURCE(S): MARPAT 137:125048
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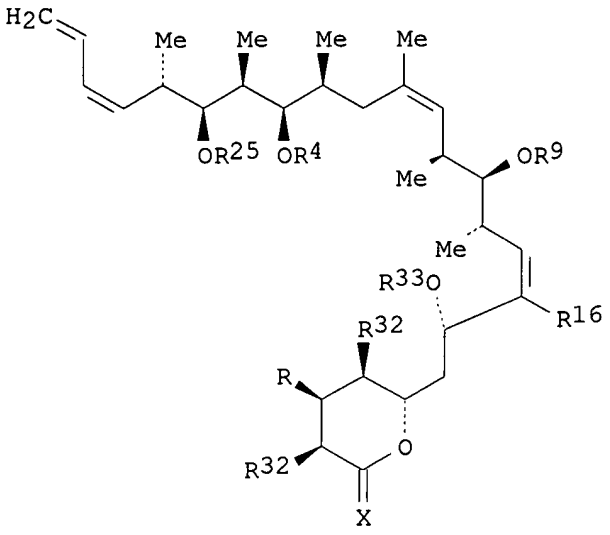


I

AB Discodermolide analogs, such as I [R = H, OR33; X = H2, O; R4, R9, R33 = H, acid labile protecting group; R25 = H, oxidatively labile protecting group; R16, R32 = H, alkyl], were prepd. Synthetic routes to both (-)- and (+)-discodermolide were presented.

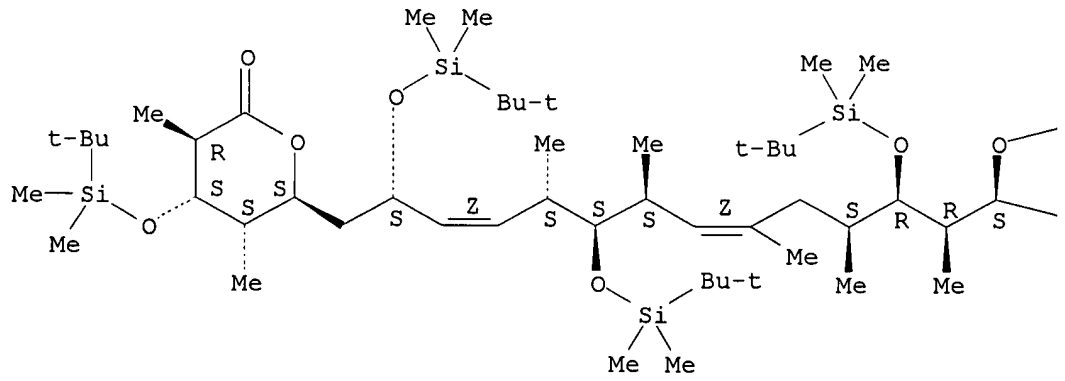
IT **252342-55-5 256921-06-9 256921-63-8 256921-65-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of compds. which mimic the chem. and biol. properties of discodermolide)

RN 252342-55-5 CAPLUS

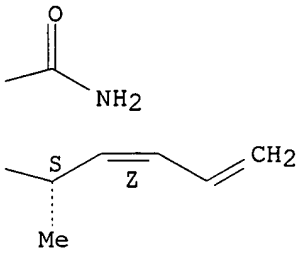
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



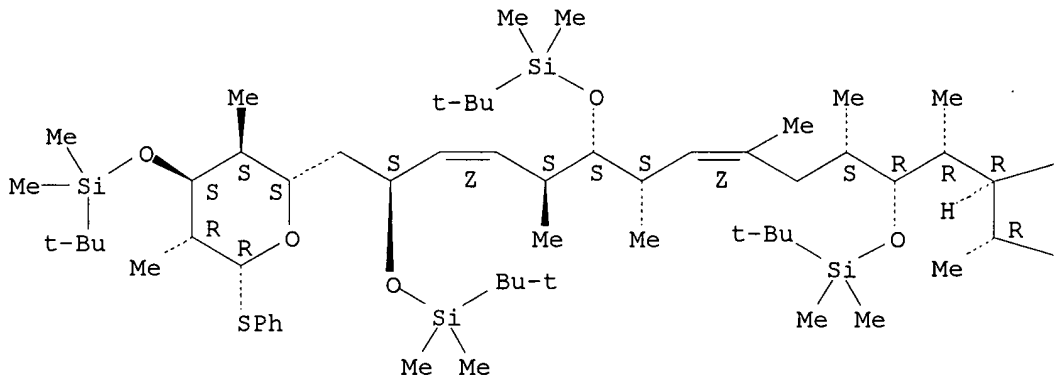
PAGE 1-B



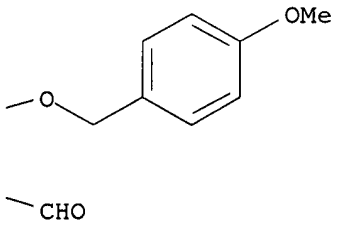
RN 256921-06-9 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

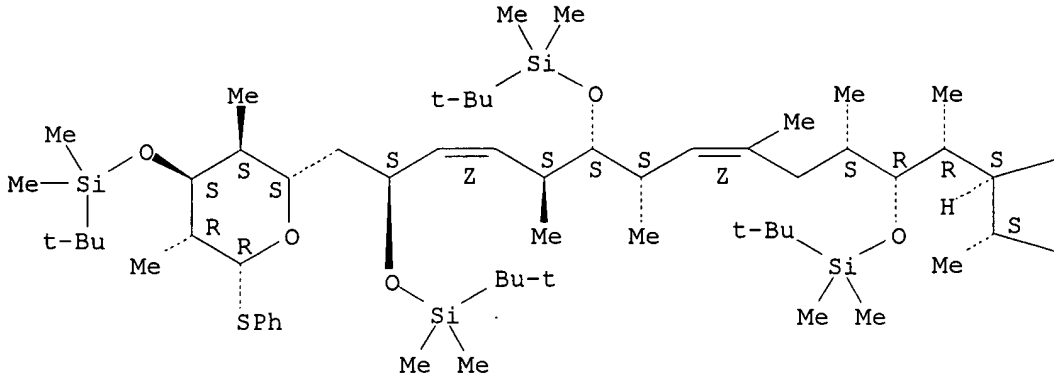


RN 256921-63-8 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-

3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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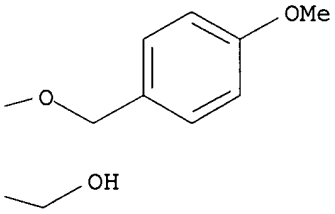
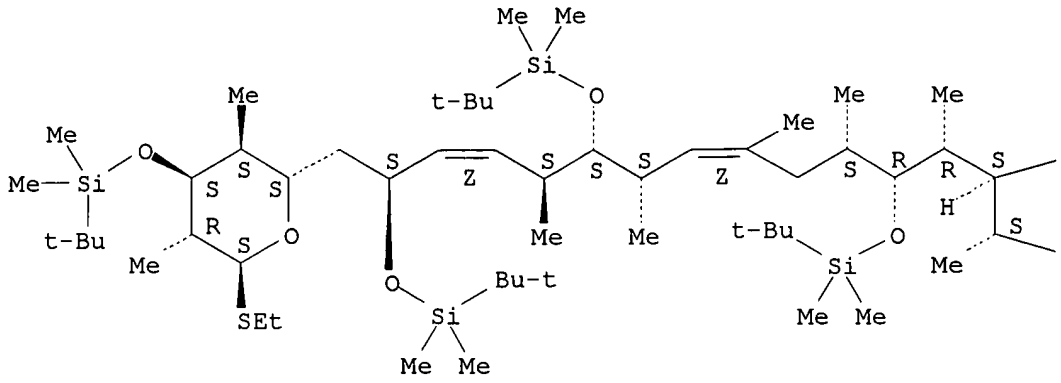


RN 256921-65-0 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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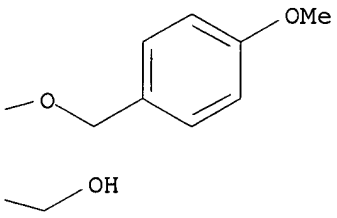

IT **208984-62-7P 208984-63-8P 208984-64-9P**
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256920-84-0P 256920-85-1P 256920-86-2P
256920-87-3P 256920-88-4P 256920-89-5P
256920-98-6P 256920-99-7P 256921-00-3P
256921-01-4P 256921-02-5P 256921-03-6P
256921-04-7P 256921-07-0P 256921-08-1P
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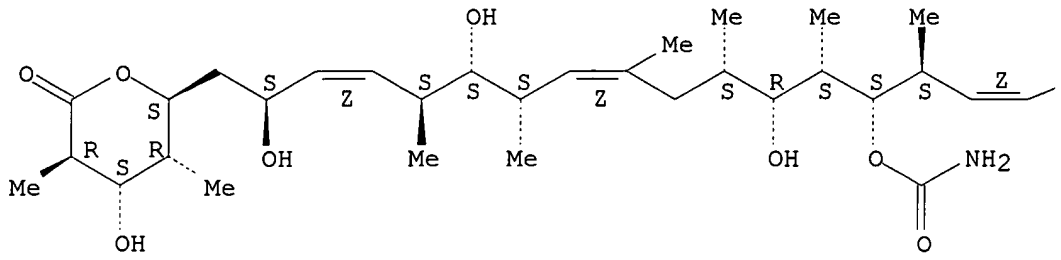
256921-40-1P 256921-41-2P 256921-42-3P
256921-43-4P 256921-44-5P 256921-45-6P
256921-46-7P 256921-47-8P 256921-50-3P
256921-51-4P 256921-52-5P 256921-60-5P
256921-61-6P 444105-62-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of compds. which mimic the chem. and biol. properties of discodermolide)

RN 208984-62-7 CAPLUS

CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4S,5S,6R,8Z,10R,11R,12R,13Z,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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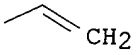


L4 ANSWER 6 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:543651 CAPLUS
TITLE: Convenient syntheses of (2R,3S,4R)-3-(tert-butyldimethylsilanyloxy)-2,4-dimethyl-5-oxopentanoic acid methoxymethylamide from methacrolein. Preparation of C1-C7 and C17-C24 fragments of (+)-discodermolide
AUTHOR(S): Day, Billy W.; Kangani, Cyrous O.; Avor, Kwasi S.
CORPORATE SOURCE: School of Pharmacy, Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA, 15261, USA
SOURCE: Tetrahedron: Asymmetry (2002), 13(11), 1161-1165
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

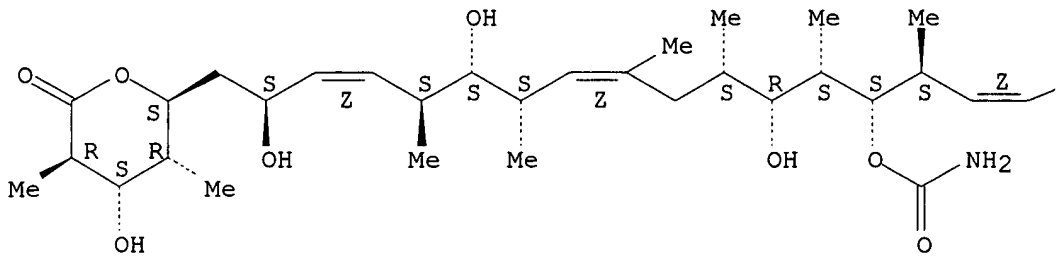
AB Two new highly stereoselective routes to (2R,3S,4R)-3-(tert-butyldimethylsilanyloxy)-2,4-dimethyl-5-oxopentanoic acid methoxymethylamide, an important intermediate in natural product synthesis, are described. Both schemes are considerably shorter and less expensive than methods previously reported. The title compd. was then converted to direct precursors of C1-C7 and C17-24 fragments of the potent microtubule stabilizer (+)-discodermolide.

IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(asym. synthesis of the direct precursors of the C1-C7 and C17-C24 fragments of (+)-discodermolide from a common oxopentanoic acid methoxy Me amide which was prepd. from methacrolein)

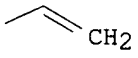
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



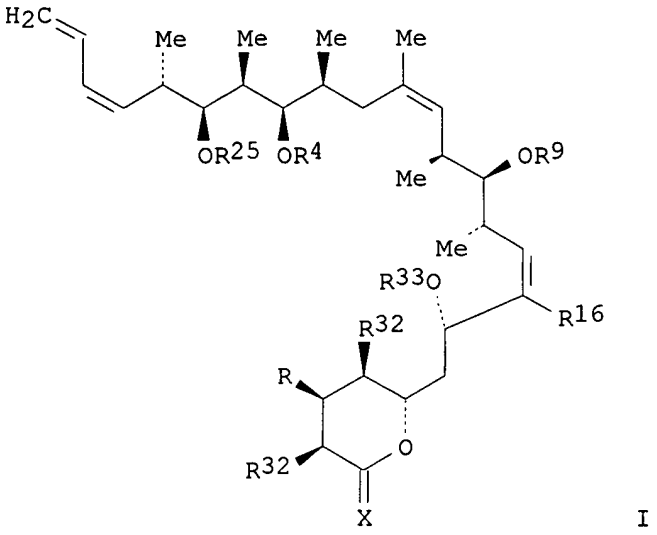
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:449643 CAPLUS
DOCUMENT NUMBER: 137:33164
TITLE: Preparation of compounds which mimic the chemical and biological properties of discodermolide
INVENTOR(S): Smith, Amos B., III; Beauchamp, Thomas J.; Lamarche, Matthew J.
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania Center for Technology Transfer, USA
SOURCE: PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046150	A2	20020613	WO 2001-US47958	20011206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002103387	A1	20020801	US 2000-730929	20001206

PRIORITY APPLN. INFO.:
US 2000-730929 A 20001206
US 1996-759817 A2 19961203
US 1998-21878 A2 19980211
US 1999-455649 A2 19991207

OTHER SOURCE(S): MARPAT 137:33164
GI



I

AB Discodermolide analogs, such as I [R = H, OR33; X = H2, O; R4, R9, R33 = H, acid labile protecting group; R25 = H, oxidatively labile protecting group; R16, R32 = H, alkyl], were prepd. Synthetic routes to both (-)- and (+)-discodermolide were presented.

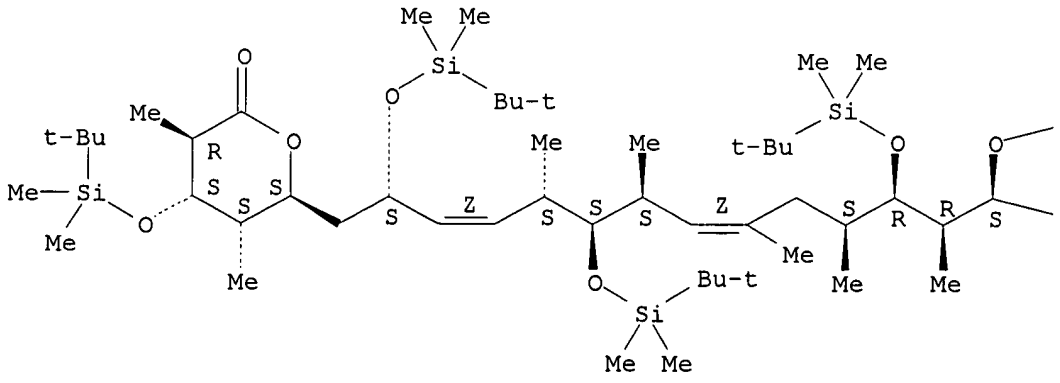
IT **252342-55-5 256921-06-9 256921-63-8 256921-65-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of compds. which mimic the chem. and biol. properties of discodermolide)

RN 252342-55-5 CAPLUS

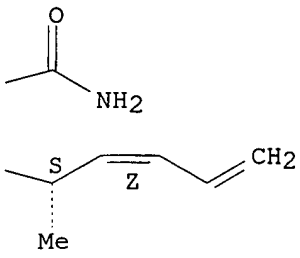
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



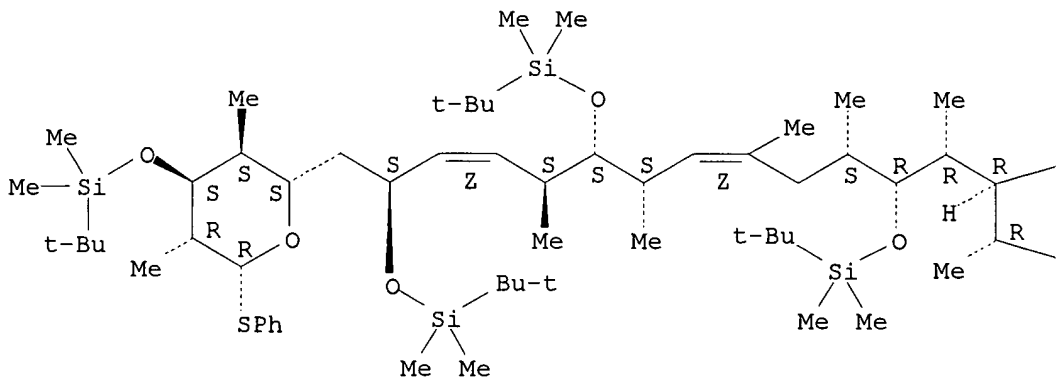
PAGE 1-B



RN 256921-06-9 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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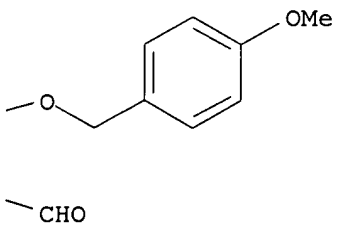
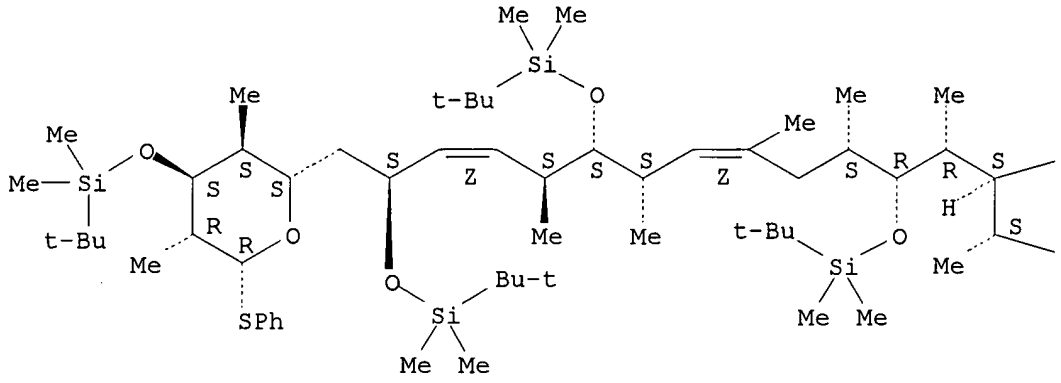


RN 256921-63-8 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-

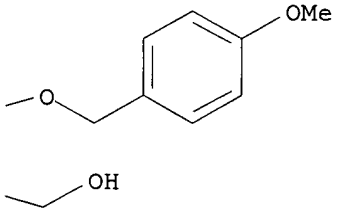
3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



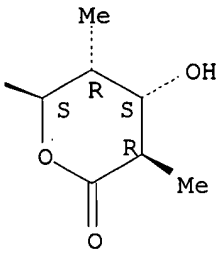
PAGE 1-B



RN 256921-65-0 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

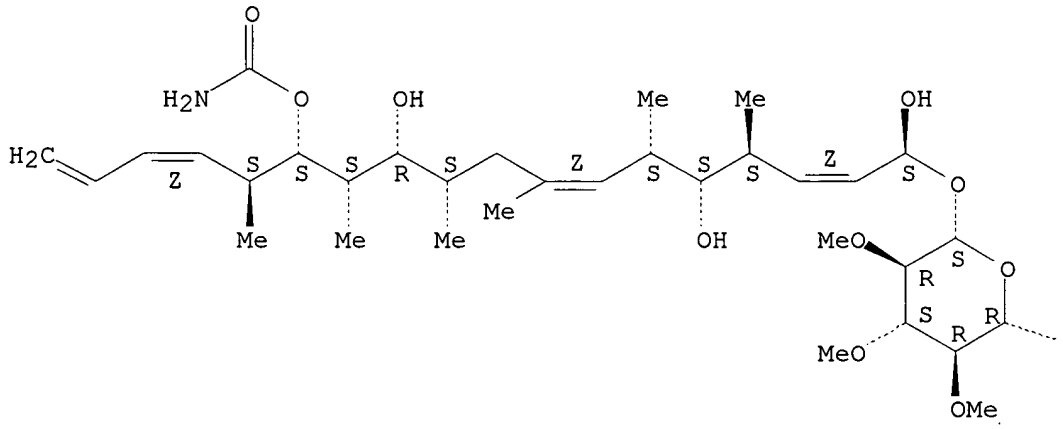
PAGE 1-B



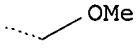
RN 256921-48-9 CAPLUS
CN .beta.-D-Glucopyranoside, (1S,2Z,4S,5S,6S,7Z,10S,11R,12S,13S,14S,15Z)-13-[(aminocarbonyl)oxy]-1,5,11-trihydroxy-4,6,8,10,12,14-hexamethyl-2,7,15,17-octadecatetraenyl 2,3,4,6-tetra-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 8 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:409254 CAPLUS

DOCUMENT NUMBER: 136:380095
TITLE: Method for treating neoplasia using combination chemotherapy
INVENTOR(S): Horwitz, Susan B.; McDaid, Hayley M.; Martello, Laura A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002065234	A1	20020530	US 2001-953585	20010914

PRIORITY APPLN. INFO.: US 2000-233191P P 20000915

AB The present invention concerns an unexpected synergistic combination of known antineoplastic agents which provides unexpectedly greater efficacy than the single agents alone. Accordingly, the present invention provides a method of treating neoplasia in a subject in need of treatment, by administering to the subject an amt. of paclitaxel effective to treat the neoplasia, in combination with an amt. of discodermolide effective to treat the neoplasia, wherein a synergistic antineoplastic effect results. The present invention further provides a synergistic combination of antineoplastic agents, comprising an effective antineoplastic amt. of paclitaxel and an effective antineoplastic amt. of discodermolide.

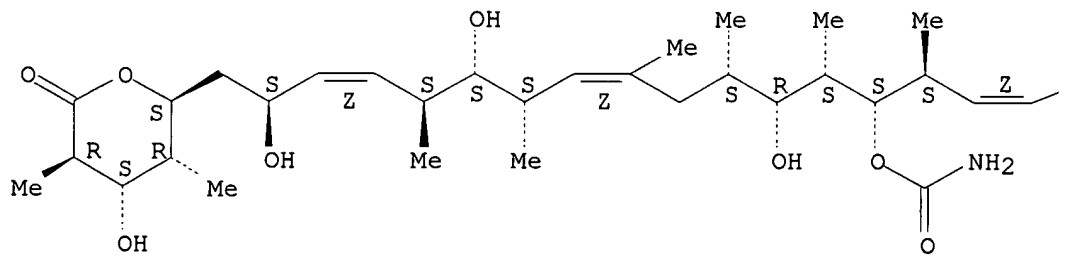
IT **127943-53-7**, Discodermolide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of neoplasia using combination chemotherapy of paclitaxel and discodermolide and resulting synergistic effects)

RN 127943-53-7 CAPLUS

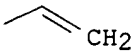
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 9 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:408776 CAPLUS
DOCUMENT NUMBER: 136:398183
TITLE: Epothilone resistant cell lines and identification of inhibiting agents and chemosensitizers
INVENTOR(S): Atadja, Peter Wisdom; Wartmann, Markus; Yan-Neale, Yan; Cohen, Dalia
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002042432	A2	20020530	WO 2001-EP13442	20011120
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2002021873	A5	20020603	AU 2002-21873	20011120

PRIORITY APPLN. INFO.: US 2000-252706P P 20001122
WO 2001-EP13442 W 20011120

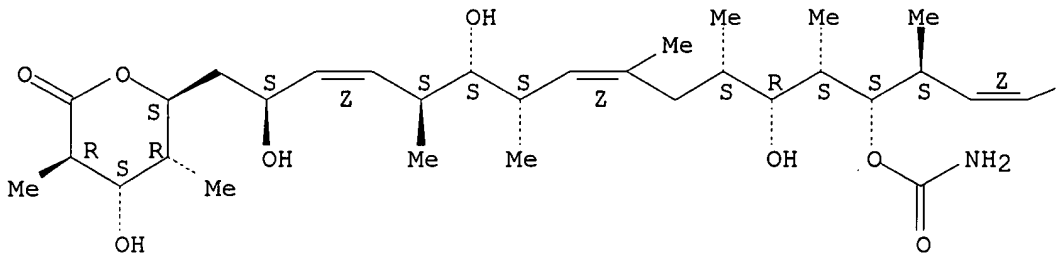
AB Epothilone resistant cells lines are disclosed. The invention also discloses methods for identifying substances which are cytotoxic to epothilone resistant cells or which are chemosensitizers or analogs of epothilone. The invention further discloses methods for identifying epothiolone resistant cells and for inhibiting the growth of epothilone resistant cells in vitro and in vivo. The invention also discloses antibodies specific for epothilone resistant cells. Also disclosed is a method to identify microtubule stabilizing agents using the epothilone resistant cell lines disclosed.

IT **127943-53-7**, Discodermolide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(epothilone resistant cell lines and identification of inhibiting agents and chemosensitizers)

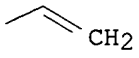
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

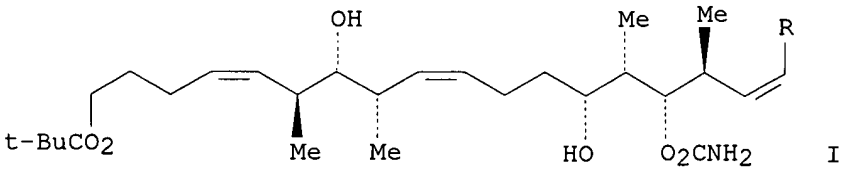


PAGE 1-B



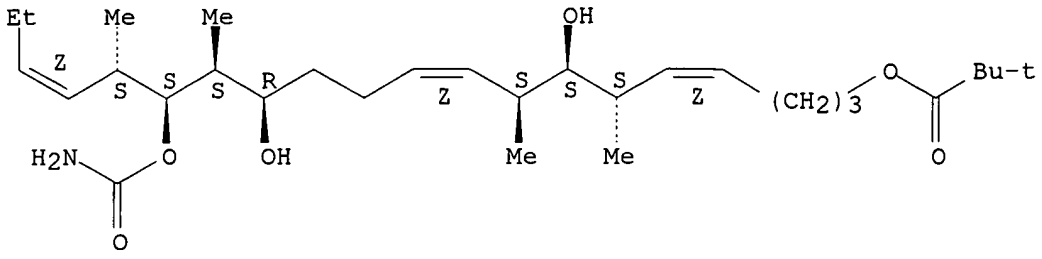
L4 ANSWER 10 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:392336 CAPLUS
DOCUMENT NUMBER: 137:140379
TITLE: Simultaneous Preparation of Four Truncated Analogues of Discodermolide by Fluorous Mixture Synthesis
AUTHOR(S): Curran, Dennis P.; Furukawa, Takashi
CORPORATE SOURCE: Department of Chemistry and Center for Combinatorial Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SOURCE: Organic Letters (2002), 4(13), 2233-2235
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:140379
GI



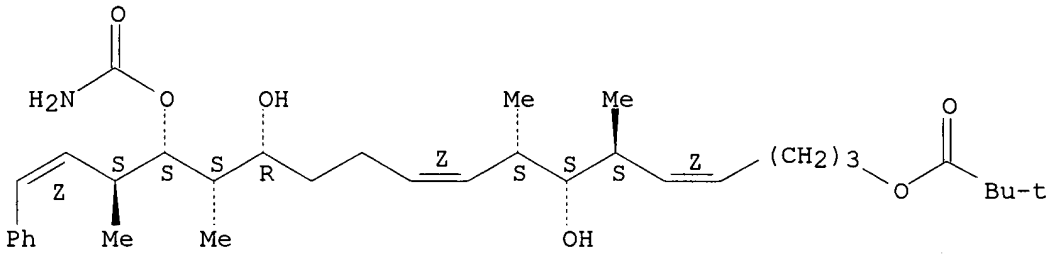
AB Four truncated analogs I (R = H, CH:CH2, Et, Ph) of the natural product discodermolide were synthesized in a single synthetic sequence. Precursors bearing four different groups at C22, each with a unique fluorous p-methoxybenzyl substituent on the C17 hydroxy group, were mixed and taken through an nine-step sequence. Demixing by fluorous chromatog. followed by deprotection and purifn. provided the individual analogs in 3-7% overall yields and with a savings of 24 synthetic steps. Fluorous mixt. synthesis is recommended as a new technique to make multiple natural product analogs in a single multistep synthesis.

IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)



RN 444682-15-9 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, (4Z,6S,7S,8S,9Z,13R,14S,15S,16S,17Z)-15-[(aminocarbonyl)oxy]-7,13-dihydroxy-6,8,14,16-tetramethyl-18-phenyl-4,9,17-octadecatrienyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:332627 CAPLUS
DOCUMENT NUMBER: 136:340539
TITLE: Preparation of bio-intermediates for use in the chemical synthesis of polyketides via fermentation using recombinant polyketide synthase
INVENTOR(S): Santi, Daniel; Ashley, Gary; Myles, David C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 69 pp., Cont.-in-part of U.S. Ser. No. 867,845.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002052028	A1	20020502	US 2001-927559	20010809
WO 2001092991	A3	20020808	WO 2001-US17352	20010529

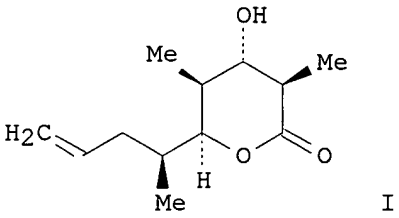
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-224038P P 20000809
US 2000-237382P P 20001004
US 2000-248387P P 20001113
US 2001-867845 A2 20010529
US 2000-207331P P 20000530

OTHER SOURCE(S): MARPAT 136:340539

GI



I

AB The present invention relates to compds., e.g. I, made by a subset of modules from one or more polyketide synthase ("PKS") genes that are used as starting material in the chem. synthesis of novel mols., particularly naturally occurring polyketides or derivs. thereof. The biol. derived intermediates ("bio-intermediates") generally represent particularly difficult compds. to synthesize using traditional chem. approaches due to one or more stereocenters. In one aspect of the invention, an intermediate in the synthesis of epothilone is provided that feeds into the synthetic protocol of Danishefsky and co-workers. In another aspect of the invention, intermediates in the synthesis of discodermolide are provided that feed into the synthetic protocol of Smith and co-workers. By taking advantage of the inherent stereochem. specificity of biol. processes, the syntheses of key intermediates and thus the overall syntheses of compds. like epothilone and discodermolide are greatly simplified.

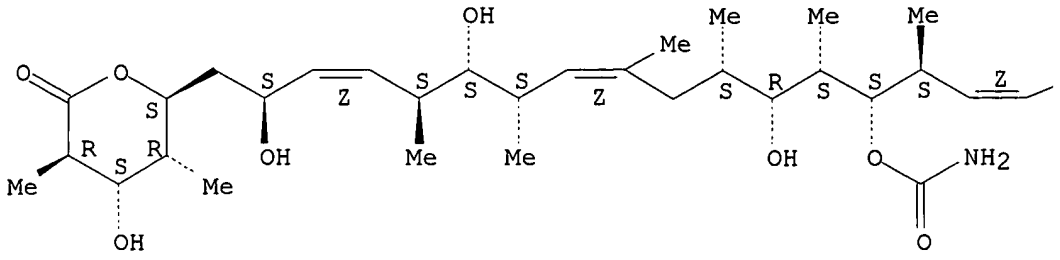
IT **127943-53-7P**, (+)-Discodermolide **398518-96-2P** **416847-07-9P** **416847-09-1P** **416847-14-8P**
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of polyketides via fermn. using recombinant polyketide synthase)

RN 127943-53-7 CAPLUS

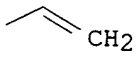
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



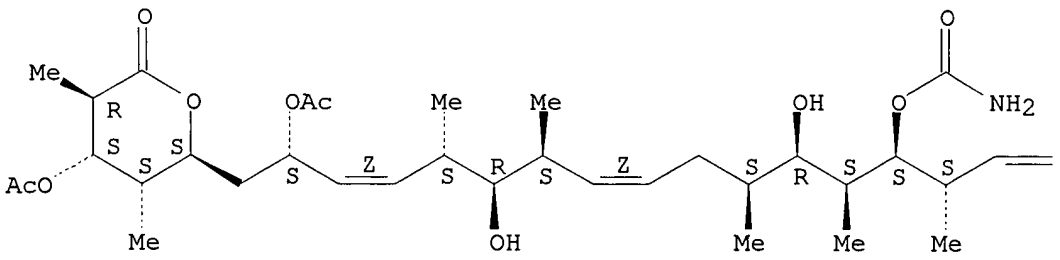
PAGE 1-B



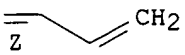
RN 398518-96-2 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,11,13,15-pentamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



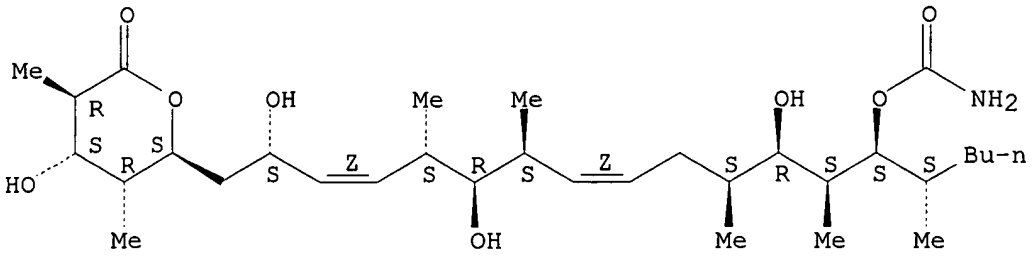
PAGE 1-B



RN 416847-07-9 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,11,13,15-pentamethyl-3,8-nonadecadienyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

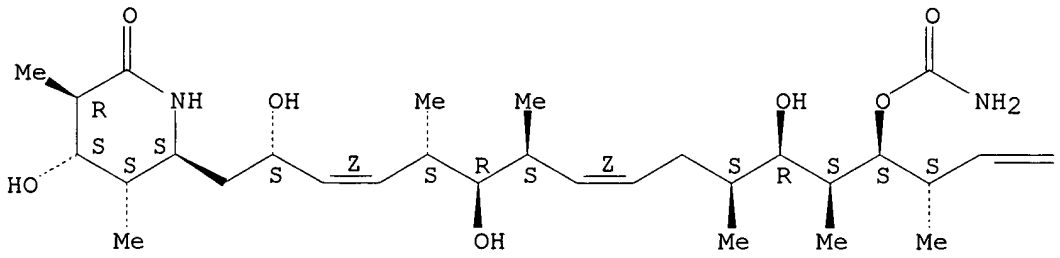
Double bond geometry as shown.



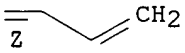
RN 416847-09-1 CAPLUS
CN 2-Piperidinone, 6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,11,13,15-pentamethyl-3,8,16,18-nonadecatetraenyl]-4-hydroxy-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



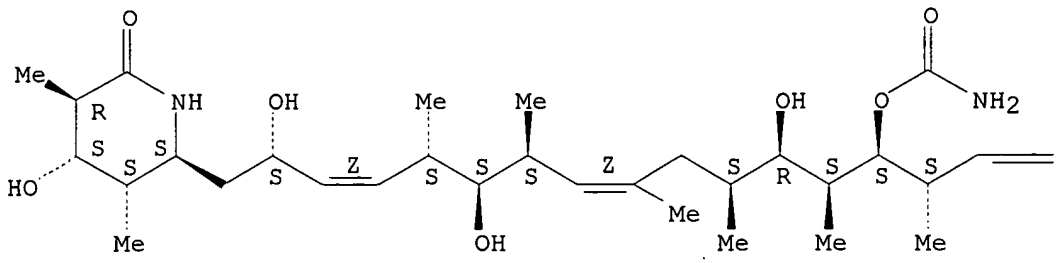
PAGE 1-B



RN 416847-14-8 CAPLUS
CN 2-Piperidinone, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-hydroxy-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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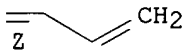


L4 ANSWER 12 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:295494 CAPLUS
DOCUMENT NUMBER: 137:109152
TITLE: Studies directed toward the synthesis of the C15-C21 fragment of (-)-discodermolide
AUTHOR(S): Chakraborty, Tushar K.; Laxman, Pasunoori
CORPORATE SOURCE: Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SOURCE: Journal of the Indian Chemical Society (2001), 78(10-12), 543-545
CODEN: JICSAH; ISSN: 0019-4522
PUBLISHER: Indian Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:109152

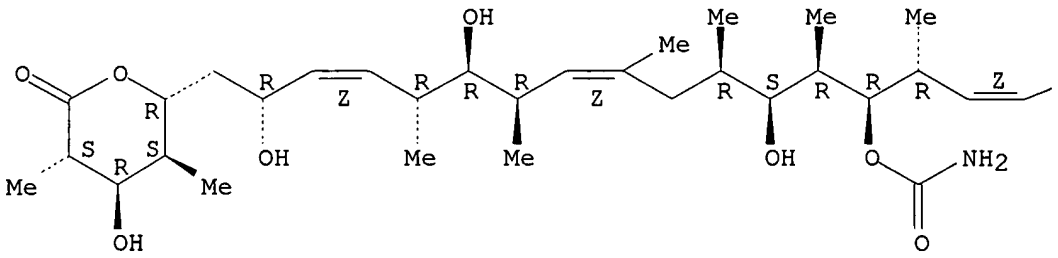
AB A novel method developed recently for the synthesis of chiral 2-methyl-1,3-diols by radical-mediated diastereoselective opening of trisubstituted epoxy alcs. at the more substituted carbon serves as the key step in the studies directed toward the stereoselective synthesis of the C15-C21 fragment of (-)-discodermolide.

IT **154335-30-5P**, (-)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(studies directed toward synthesis of C15-C21 fragment of (-)-discodermolide)

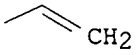
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:288666 CAPLUS
DOCUMENT NUMBER: 137:179507
TITLE: Differential mitotic responses to microtubule-stabilizing and -destabilizing drugs
AUTHOR(S): Chen, Jie-Guang; Horwitz, Susan Band
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: Cancer Research (2002), 62(7), 1935-1938
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

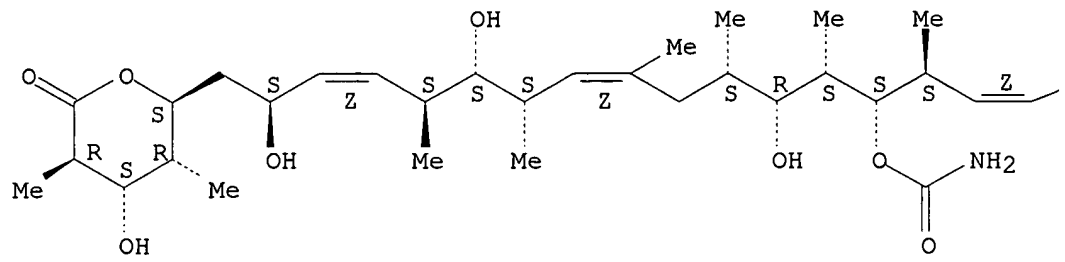
AB Although microtubule interacting agents inhibit spindle dynamics, thereby leading to a block in mitosis, we report that low concns. of these drugs result in differential mitotic effects. Microtubule-stabilizing agents including Taxol, epothilone B, and discodermolide produce aneuploid populations of A549 cells in the absence of a mitotic block. Such aneuploid populations are diminished in an epothilone B-resistant cell line. In contrast, microtubule-destabilizing agents like colchicine, nocodazole, and vinblastine are unable to initiate aneuploidy. The aneuploid cells result from aberrant mitosis as multipolar spindles are induced by the stabilizing drugs, but not by destabilizing agents. The results suggest that the mechanism underlying aberrant mitosis may not be the same as that responsible for mitotic block, and that the former dets. the sensitivity of cells to Taxol-like drugs.

IT **127943-53-7**, Discodermolide
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential mitotic responses to microtubule-stabilizing and -destabilizing drugs)

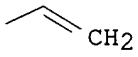
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:256023 CAPLUS
DOCUMENT NUMBER: 136:299699
TITLE: Emulsion vehicle for poorly soluble drugs
INVENTOR(S): Constantinides, Panayiotis P.; Lambert, Karel J.; Tustian, Alexander K.; Nienstedt, Andrew M.; Hartgraves, Greg A.
PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026208	A2	20020404	WO 2001-US30471	20010927
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001093177	A5	20020408	AU 2001-93177	20010927

PRIORITY APPLN. INFO.: US 2000-670627 A1 20000927
WO 2001-US30471 W 20010927

AB Pharmaceutical compns. contain one or more therapeutics or chemotherapeutics, one or more tocols as a solvent, a surfactant, and optionally a co-solvent. An example was given in which paclitaxel was

solubilized with .alpha.-tocopherol.

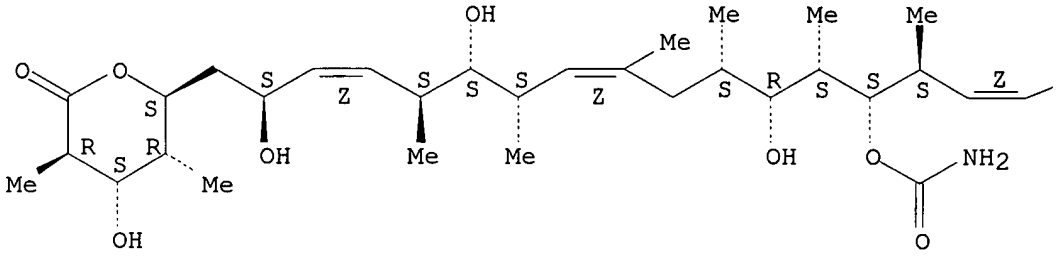
IT **127943-53-7**, Discodermolide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(emulsion vehicle for poorly sol. drugs)

RN 127943-53-7 CAPLUS

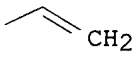
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 15 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:157495 CAPLUS
DOCUMENT NUMBER: 136:205412
TITLE: Oligopeptide-based prodrugs activated by plasmin and their use in cancer chemotherapy
INVENTOR(S): Trouet, Andre; Dubois, Vincent; Passioukov, Alexandre
PATENT ASSIGNEE(S): Coulter Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015700	A1	20020228	WO 2001-US26476	20010823

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001086727 A5 20020304 AU 2001-86727 20010823
PRIORITY APPLN. INFO.: US 2000-227686P P 20000824
WO 2001-US26476 W 20010823
OTHER SOURCE(S): MARPAT 136:205412

AB A prodrug, cleavable by plasmin, comprises a therapeutic agent capable of entering a target cell, e.g., a tumor or inflammatory cell, an oligopeptide having a plasmin peptide substrate of 2-4 amino acids and mono- or di-peptide linkage, a stabilizing group and, optionally, a linker group. Also disclosed are methods of making and using the prodrug compds. For example, the activity of D-Ala-Leu-Lys-Leu-Leu-doxorubicin (I) (prepn. given) was evaluated in the B16-B16 murine melanoma model. The mice receiving the prodrug did not show any important wt. loss during the expt. and no clin. signs of toxicity were obsd. At the same time, the drug had a marked effect on the metastatic growth. At 34.5 .mu.mol/kg, I reduced the spread of lung metastases with a decrease of the ratio of the surface occupied by B16-B16 colonies to the non-affected one to 8.2.+-.1.8% (P<0.01), compared to 45.7.+-.12.6% and 44.0.+-.6.3% for non-treated and doxorubicin (5.2 .mu.mol/kg)-treated animals. The same prodrug at 69.0 .mu.mol/kg provided 1.5.+-.0.6% of surface affected.

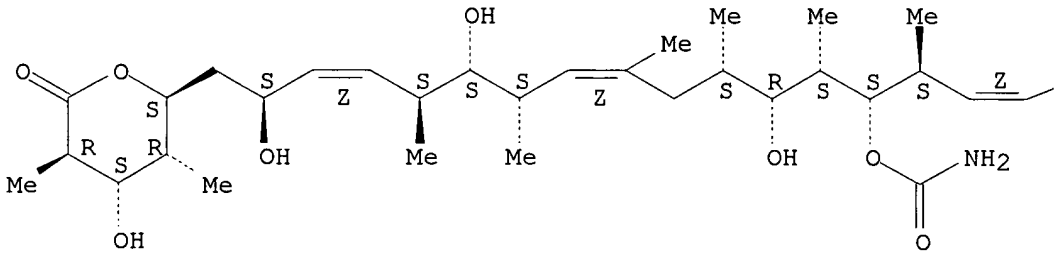
IT **127943-53-7**, Discodermolide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oligopeptide-based prodrugs activated by plasmin for chemotherapy)

RN 127943-53-7 CAPLUS

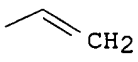
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:132139 CAPLUS
DOCUMENT NUMBER: 136:303707
TITLE: Discodermolide and taxol: a synergistic drug combination in human carcinoma cell lines
AUTHOR(S): Horwitz, Susan Band; Martello, Laura A.; Yang,

Chia-Ping H.; Smith, Amos B., III; McDaid, Hayley M.
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: ACS Symposium Series (2001), 796(Anticancer Agents), 81-96
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New natural products with Taxol-like activities have been identified during a search for compds. with the same mechanism of action as Taxol, but with better therapeutic properties. The epothilones, eleutherobin and discodermolide, like Taxol, all enhance the polymn. of stable microtubules. Careful analyses of these compds. have indicated that Taxol and discodermolide have differential effects in cells. The presence of low concns. of Taxol significantly increased the cytotoxicity of discodermolide. Median effect anal., using the combination index method, revealed a schedule-independent synergistic interaction between Taxol and discodermolide in human carcinoma cell lines, suggesting that these two drugs could represent an important drug combination in the treatment of cancer.

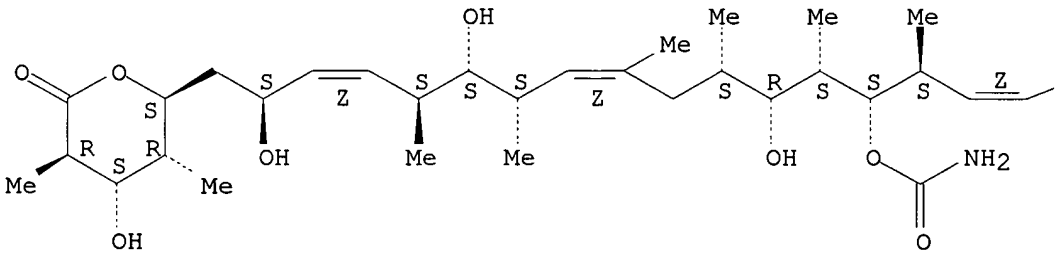
IT **127943-53-7**, Discodermolide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic combination of discodermolide and taxol against human carcinoma cell lines)

RN 127943-53-7 CAPLUS

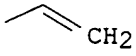
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

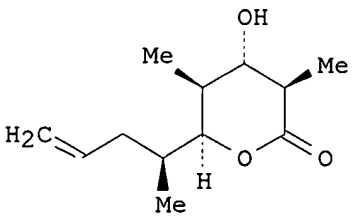
L4 ANSWER 17 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:123244 CAPLUS

DOCUMENT NUMBER: 136:183657
TITLE: Process for the biomediated preparation of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide
INVENTOR(S): Santi, Daniel V.; Ashley, Gary; Myles, David C.
PATENT ASSIGNEE(S): Kosan Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012534	A2	20020214	WO 2001-US25112	20010809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2001092991	A3	20020808	WO 2001-US17352	20010529
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001083275	A5	20020218	AU 2001-83275	20010809

PRIORITY APPLN. INFO.:
US 2000-224038P P 20000809
US 2000-237382P P 20001004
US 2000-248387P P 20001113
US 2001-867845 A 20010529
US 2000-207331P P 20000530
WO 2001-US25112 W 20010809

OTHER SOURCE(S): CASREACT 136:183657; MARPAT 136:183657
GI



I

AB The present invention relates to compds., such as I, made by a subset of modules from one or more polyketide synthase ("PKS") genes that are used as starting material in the chem. synthesis of novel mols., particularly

naturally occurring polyketides or derivs. thereof. The biol. derived intermediates ("bio-intermediates") generally represent particularly difficult compds. to synthesize using traditional chem. approaches due to one or more stereocenters. In one aspect of the invention, an intermediate in the synthesis of epothilone is provided that feeds into the synthetic protocol of Danishefsky and co-workers. In another aspect of the invention, intermediates in the synthesis of discodermolide are provided that feed into the synthetic protocol of Smith and co-workers. By taking advantage of the inherent stereochem. specificity of biol. processes, the syntheses of key intermediates and thus the overall syntheses of compds. like epothilone and discodermolide are greatly simplified.

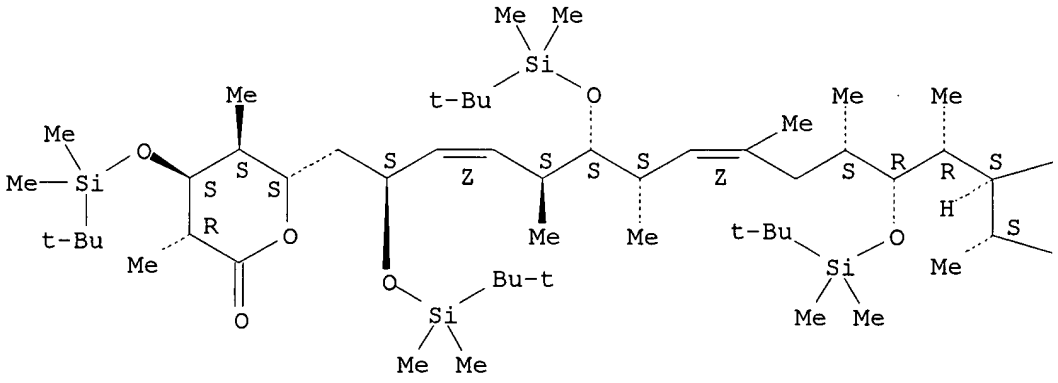
IT **252342-47-5P 252342-48-6P 252342-55-5P**
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(process for the biomediated prepn. of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide)

RN 252342-47-5 CAPLUS

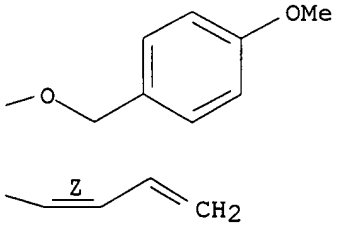
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



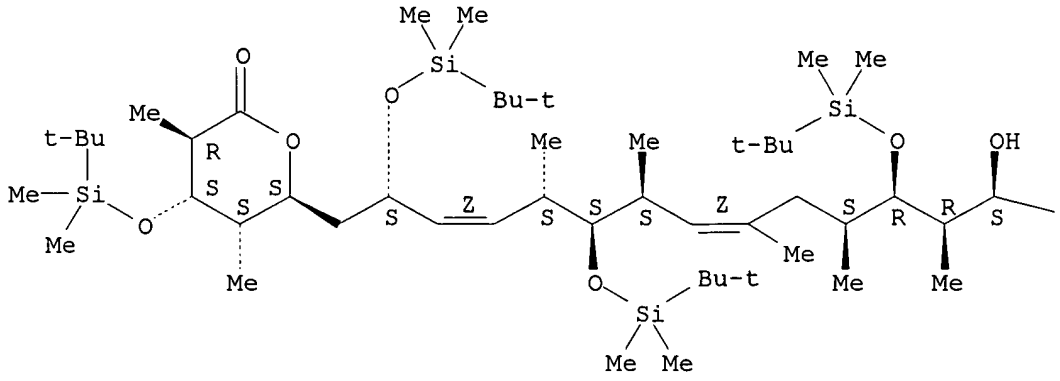
PAGE 1-B



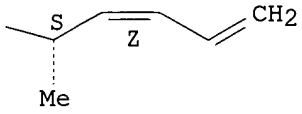
RN 252342-48-6 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



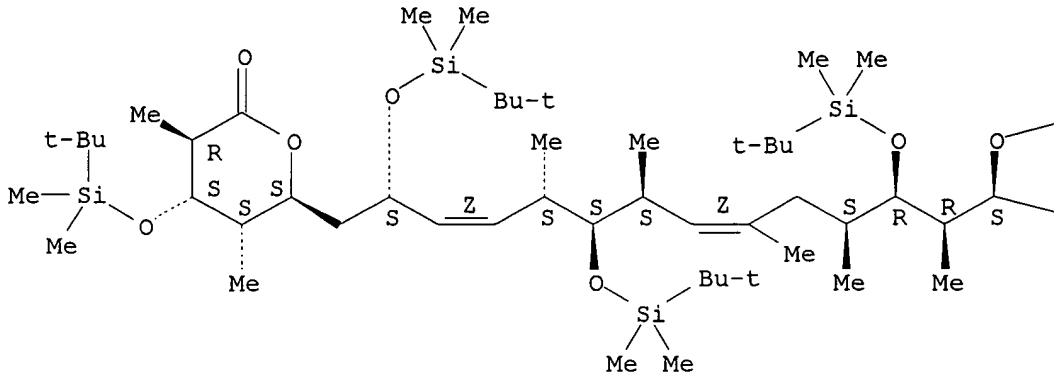
PAGE 1-B



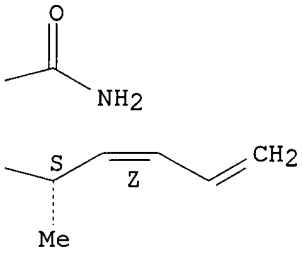
RN 252342-55-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



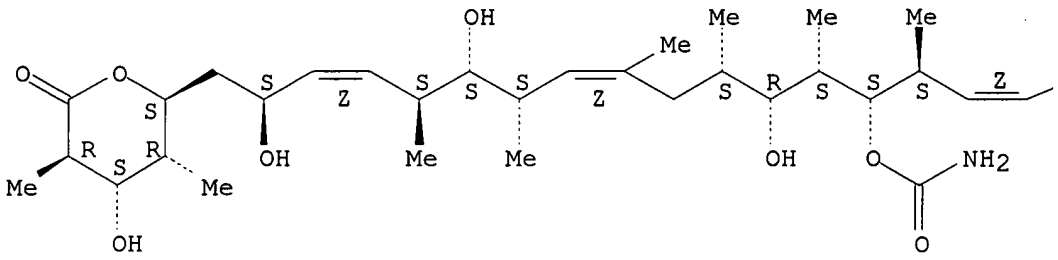
IT **127943-53-7P**, Discodermolide **192187-47-6P**
389056-34-2P 398518-96-2P 398518-98-4P
398519-00-1P
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); IMF (Industrial manufacture); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(process for the biomediated prepn. of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide)

RN 127943-53-7 CAPLUS

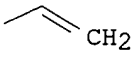
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

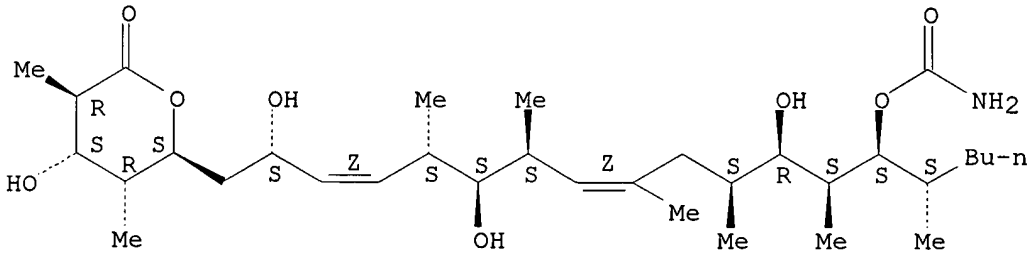


PAGE 1-B



RN 192187-47-6 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8-nonadecadienyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

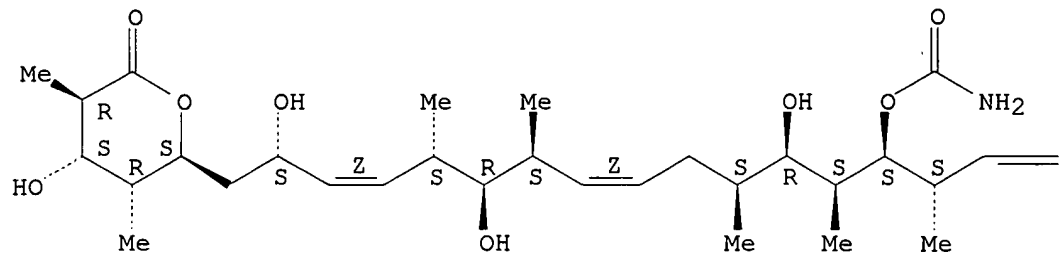
Absolute stereochemistry.
Double bond geometry as shown.



RN 389056-34-2 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,11,13,15-pentamethyl-3,8,16,18-nonatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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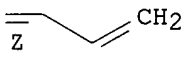
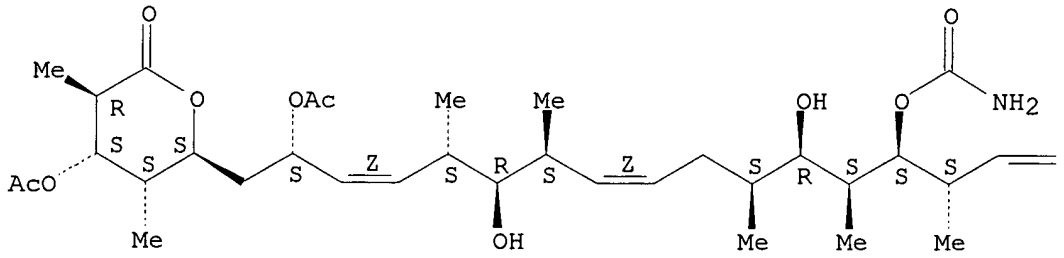


RN 398518-96-2 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,11,13,15-pentamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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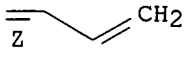
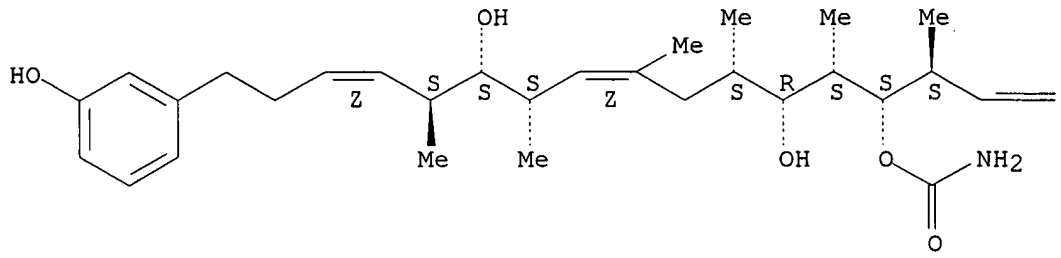


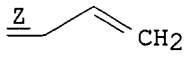
RN 398518-98-4 CAPLUS
CN 1,3,11,16-Nonadecatetraene-6,8,14-triol, 19-(3-hydroxyphenyl)-5,7,9,11,13,15-hexamethyl-, 6-carbamate, (3Z,5S,6S,7S,8R,9S,11Z,13S,14S,15S,16Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



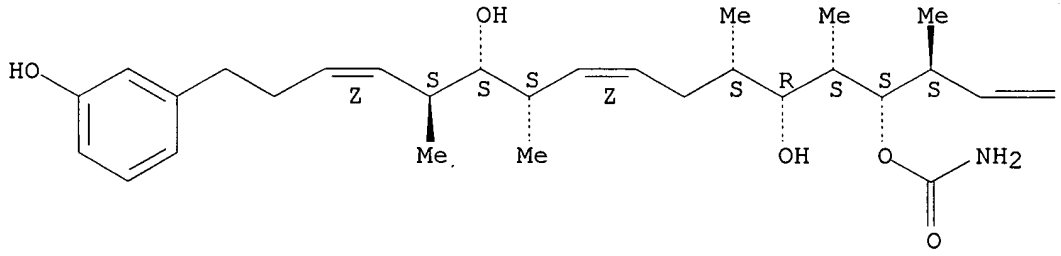
PAGE 1-B



RN 398519-00-1 CAPLUS
CN 1,3,11,16-Nonadecatetraene-6,8,14-triol, 19-(3-hydroxyphenyl)-5,7,9,13,15-pentamethyl-, 6-carbamate, (3Z,5S,6S,7S,8R,9S,11Z,13S,14S,15S,16Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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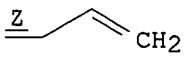
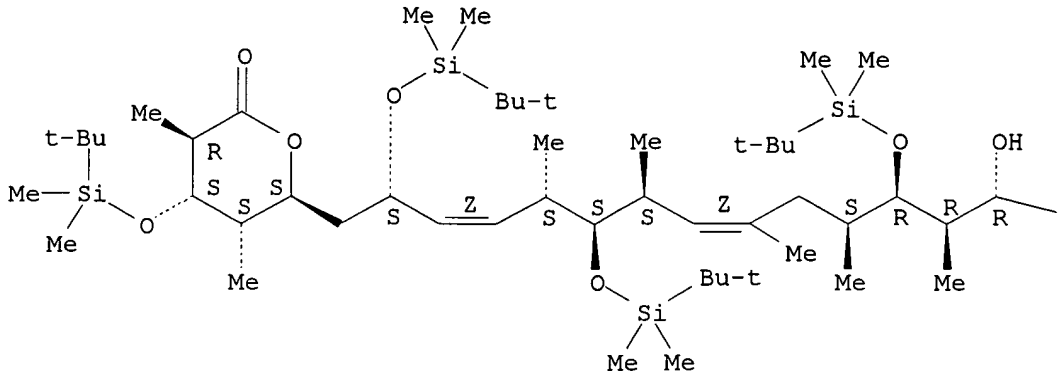


IT **398519-21-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the biomediated prepn. of intermediates for use in the synthesis of polyketides, such as epothilone D and discodermolide)
RN 398519-21-6 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14R,15S,16Z)-2,6,12-tris[[(1,1-

dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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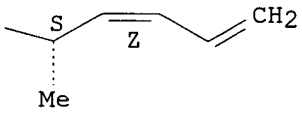


L4 ANSWER 18 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:122985 CAPLUS
DOCUMENT NUMBER: 136:167219
TITLE: Process for the preparation of discodermolide and analogues thereof
INVENTOR(S): Kinder, Frederick Ray
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012220	A2	20020214	WO 2001-EP9068	20010806
WO 2002012220	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001093726 A5 20020218 AU 2001-93726 20010806

PRIORITY APPLN. INFO.: US 2000-633753 A 20000807
WO 2001-EP9068 W 20010806

OTHER SOURCE(S): CASREACT 136:167219; MARPAT 136:167219

AB A more practical synthesis for prepg. (+)-discodermolide and structurally related analogs via a stereoselective aldol condensation/redn. sequence was presented.

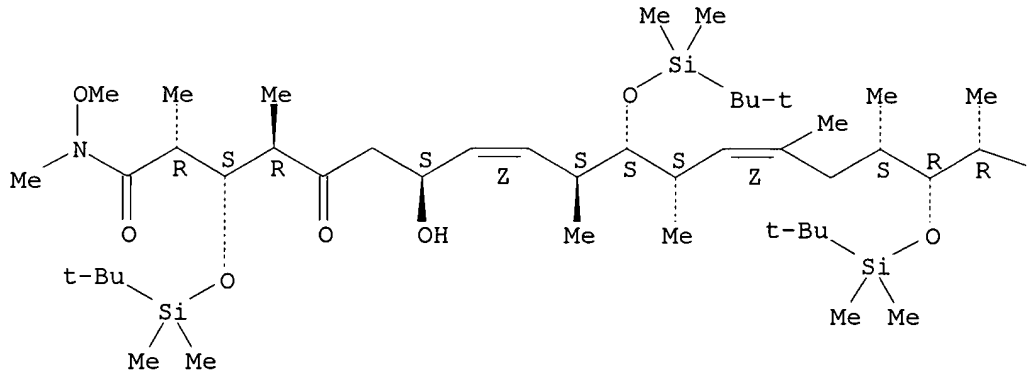
IT **397331-44-1P 397331-45-2P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for the prepn. of discodermolide and analogs thereof)

RN 397331-44-1 CAPLUS

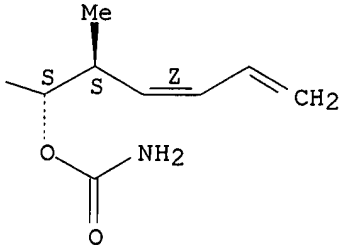
CN 8,13,21,23-Tetracosatetraenamide, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-N-methoxy-N,2,4,10,12,14,16,18,20-nonamethyl-5-oxo-, (2R,3S,4R,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



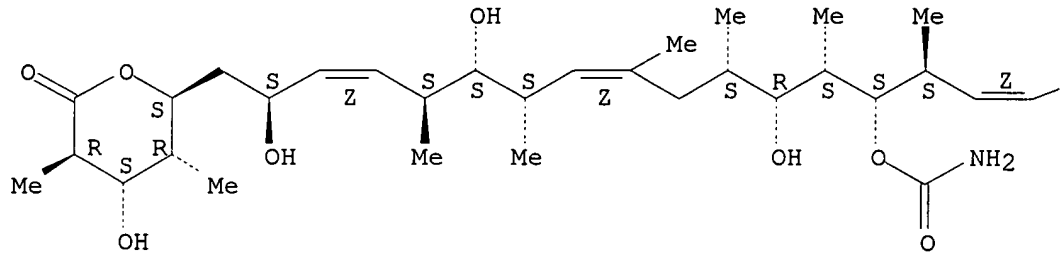
PAGE 1-B



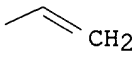
nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



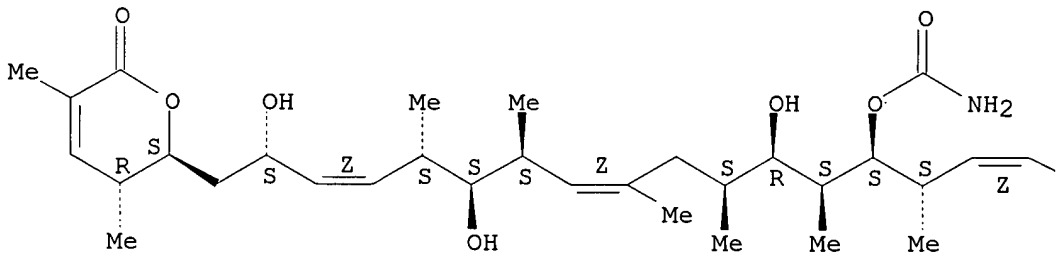
PAGE 1-B



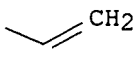
RN 358968-14-6 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

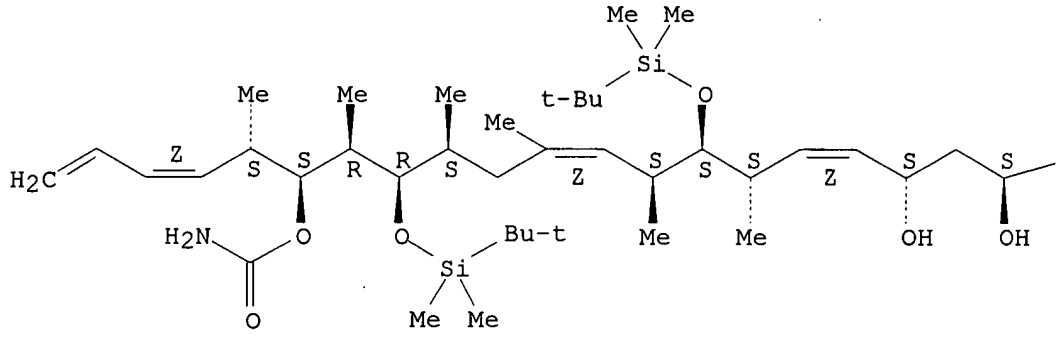


RN 389056-34-2 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6R,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-

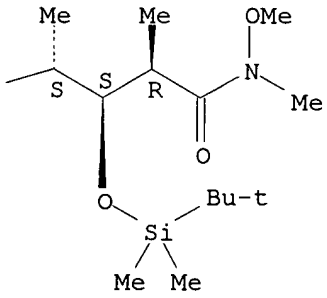
RN 397331-45-2 CAPLUS
CN 8,13,21,23-Tetracosatetraenamide, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-N-methoxy-N,2,4,10,12,14,16,18,20-nonamethyl-, (2R,3S,4S,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



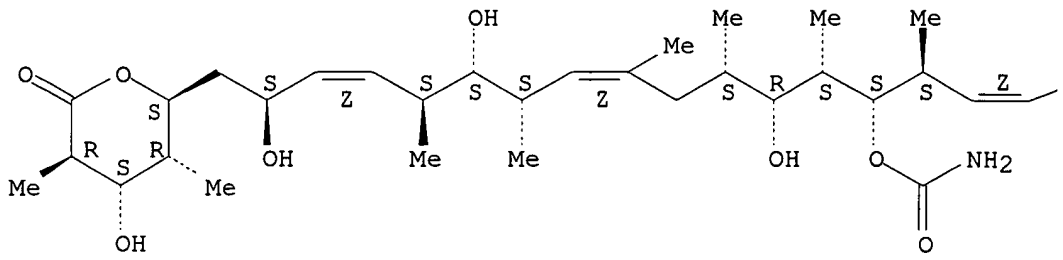
PAGE 1-B



IT **127943-53-7P**, (+)-Discodermolide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the prepn. of discodermolide and analogs thereof)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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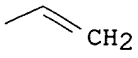
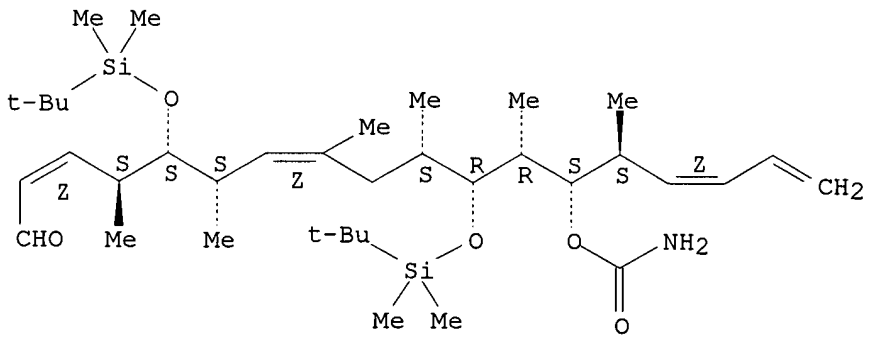


IT **261968-08-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for the prepn. of discodermolide and analogs thereof)
RN 261968-08-5 CAPLUS
CN 2,7,15,17-Octadecatetraenal, 13-[(aminocarbonyl)oxy]-5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L4 ANSWER 19 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:8664 CAPLUS
DOCUMENT NUMBER: 137:41358
TITLE: Taxol and discodermolide: functional similarities and differences
AUTHOR(S): Martello-Rooney, Laura
CORPORATE SOURCE: Yeshiva Univ., New York, NY, USA
SOURCE: (2001) 174 pp. Avail.: UMI, Order No. DA3003077
From: Diss. Abstr. Int., B 2001, 62(2), 799
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7**, Discodermolide

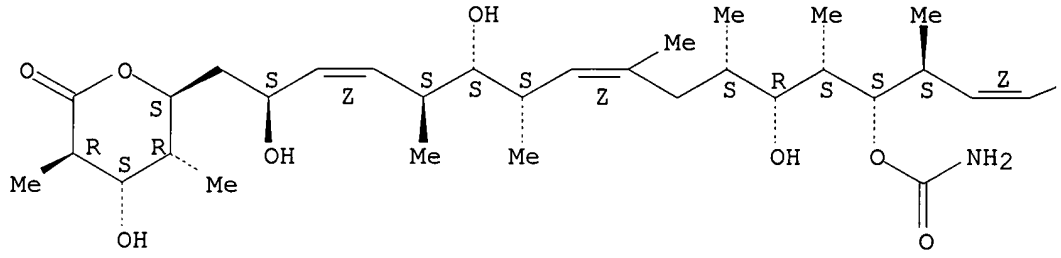
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Taxol and discodermolide as tumor inhibitors in relation to combination therapy and resistance and interaction with tubulins)

RN 127943-53-7 CAPLUS

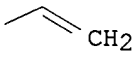
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 20 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:885823 CAPLUS
DOCUMENT NUMBER: 136:42834
TITLE: Tumor activated prodrug compounds
INVENTOR(S): Trouet, Andre; Dubois, Vincent; Oronsky, Arnold
PATENT ASSIGNEE(S): Universite Catholique De Louvain, Belg.
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001091798	A2	20011206	WO 2001-EP6106	20010529

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-208996P P 20000601

EP 2000-870130 A 20000615
EP 2000-870306 A 20001218

OTHER SOURCE(S): MARPAT 136:42834

AB The invention is directed to novel prodrug compds., compns. comprising the prodrugs, methods of making and using them. The prodrugs comprise a biol. active entity linked to a masking moiety via a linking moiety. The prodrug compds. are selectively activated at or near target cells and display lower toxicity and possibly a longer in vivo or serum half-life than the corresponding naked biol. active entity. A IGF-1 antagonist is used to prep. a dual prodrug with doxorubicin. For the dual prodrug, conjugation takes place at the carboxyterminus of the antagonist rather than on its free N-terminal amino group. The in vivo toxicity of the dual prodrug is evaluated, and its chemotherapeutic activity is compared to that of Dox and of the IGF-1 antagonist, alone or in combination.

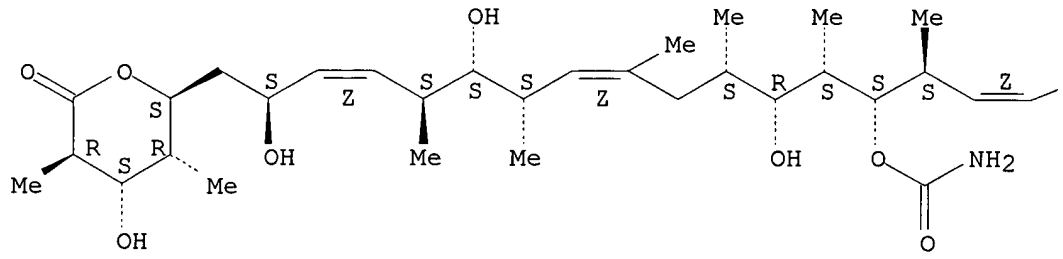
IT **127943-53-7D**, Discodermolide, prodrugs
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor activated prodrug compds.)

RN 127943-53-7 CAPLUS

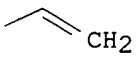
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 21 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:823665 CAPLUS
DOCUMENT NUMBER: 136:118320
TITLE: Efficient Strategy for the Synthesis of Stereopentad Subunits of Scytophycin, Rifamycin S, and Discodermolide
AUTHOR(S): BouzBouz, S.; Cossy, J.
CORPORATE SOURCE: Laboratoire de Chimie Organique, ESPCI, Paris, 75231, Fr.
SOURCE: Organic Letters (2001), 3(25), 3995-3998
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

AB An efficient, simple method has been developed for the stereocontrolled synthesis of polypropionate stereopentads, present in the natural products scytophycin, rifamycin S, and discodermolide, in high enantio- and diastereomeric purities.

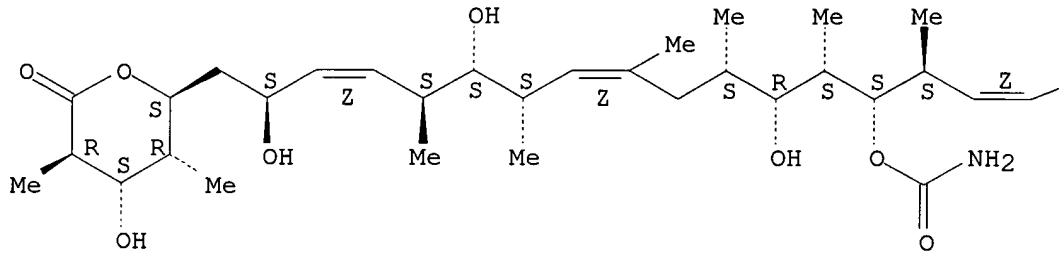
IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(efficient strategy for the synthesis of stereopentad subunits of scytophycin, rifamycin S, and discodermolide)

RN 127943-53-7 CAPLUS

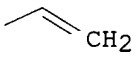
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:810474 CAPLUS
DOCUMENT NUMBER: 137:87639
TITLE: Novel molecules that interact with microtubules and have functional activity similar to Taxol
AUTHOR(S): He, Lifeng; Orr, George A.; Horwitz, Susan Band
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: Drug Discovery Today (2001), 6(22), 1153-1164
CODEN: DDTOFS; ISSN: 1359-6446
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Taxol is an antitumor drug approved by the FDA for the treatment of ovarian, breast and non-small-cell lung carcinomas. Originally isolated from the bark of the Pacific yew, Taxus brevifolia, it was the first natural product described that stabilized microtubules. In the past five years, a group of novel natural products, including the epothilones, discodermolide, eleutherobin, sarcodictyins and the

laulimalides, all of which have biol. activities similar to those of Taxol, has been discovered. In this review, we discuss each of these novel microtubule-stabilizing agents and the search for a common pharmacophore among them, taking into consideration recent advances in our understanding of the taxanes and tubulin.

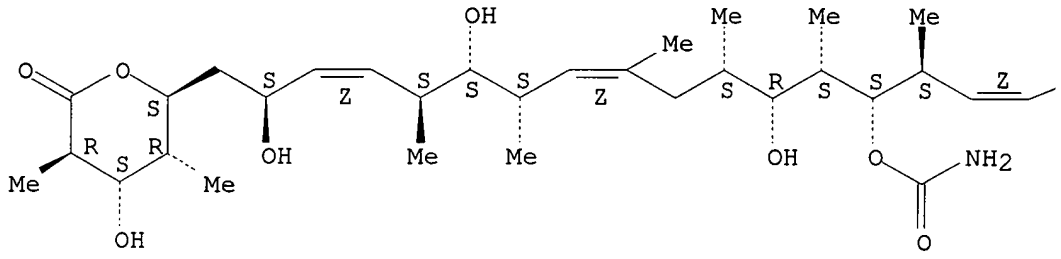
IT **127943-53-7**, (+)-Discodermolide **154335-30-5**, (-)-Discodermolide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel mols. that interact with microtubules and have functional activity similar to Taxol)

RN 127943-53-7 CAPLUS

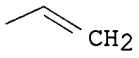
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

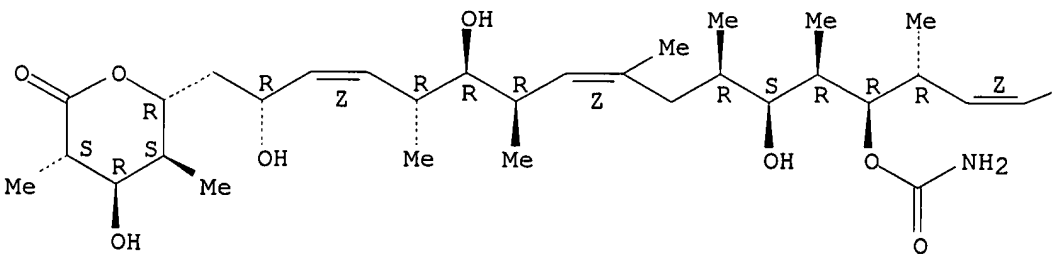


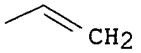
RN 154335-30-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





L4 ANSWER 23 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:747604 CAPLUS
DOCUMENT NUMBER: 135:298766
TITLE: Method for treating multidrug resistant cells with antitumor discodermolide
INVENTOR(S): Lassota, Peter; Jagoe, Christopher T.
PATENT ASSIGNEE(S): Novartis Ag, Switz.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074355	A1	20011011	WO 2000-US8904	20000404

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

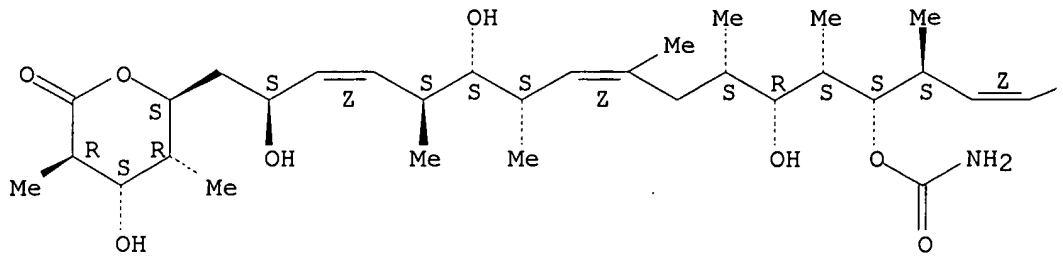
AB The present invention relates to methods for treating multidrug resistant cells, preferably multidrug resistant cancer cells, with discodermolide. Discodermolide is found to be effective in limiting the growth of otherwise growth unregulated cells having .beta.-tubulin mutations and in promoting phosphorylation of the oncogene RAF-1.

IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor discodermolide is effective in treating multidrug resistant cancer cells)

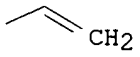
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:730715 CAPLUS
DOCUMENT NUMBER: 135:288636
TITLE: Synergistic methods and compositions for treating cancer using two or more anticancer agents
INVENTOR(S): Lee, Francis Y.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

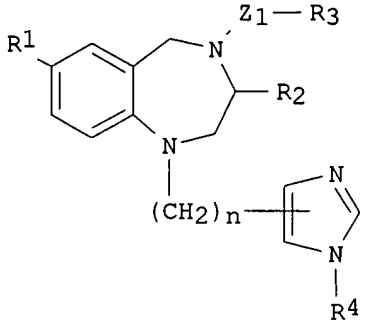
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072721	A2	20011004	WO 2001-US9193	20010322
WO 2001072721	A3	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002002162	A1	20020103	US 2001-817456	20010326

PRIORITY APPLN. INFO.: US 2000-192278P P 20000327
OTHER SOURCE(S): MARPAT 135:288636
GI



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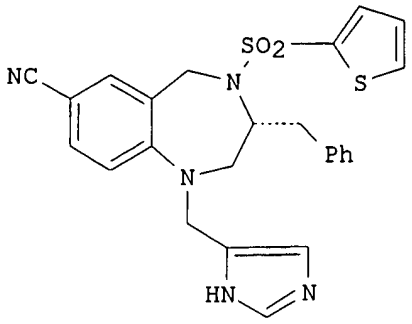


II

AB The present invention provides a synergistic method for the treatment of cancer which comprises administering a synergistically, therapeutically effective amt. of: (i) at least agent selected from the group consisting of cytotoxic agents and cytostatic agents, and (ii) a compd. of formula [I; R1 = Cl, Br, CN, substituted Ph, substituted pyridyl; R2 = alkyl, aralkyl; R3,R5 = substituted alkyl, aryl, heterocycle; R4 = H, alkyl; Z1 = CO, SO2, CO2, SO2N(R5); n = 1,2] or a pharmaceutically acceptable salt thereof. The present invention further provides a pharmaceutical compn. for the synergistic treatment of cancer which comprises at least one agent selected from the group consisting of antiproliferative cytotoxic agents and antiproliferative cytostatic agents, a compd. of formula I, and a pharmaceutically acceptable carrier. Synergism was obsd. when non-proliferating tumor cells were treated with diazepine II.cntdot.HCl and paclitaxel (III) simultaneously or when III preceded II.cntdot.HCl.

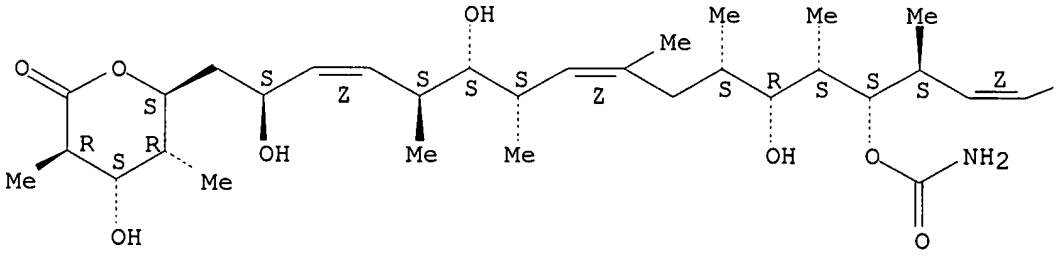
IT **127943-53-7**, Discodermolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic methods using two or more anticancer agents for treating cancer)

RN 127943-53-7 CAPLUS

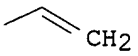
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 25 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:694007 CAPLUS
DOCUMENT NUMBER: 136:5848
TITLE: Versatile, high 2,4-syn dialkyl diastereoselection in the radical debromination of .alpha.-bromo-.alpha.-methyl-.delta.-valerolactones with tri-n-butyltin hydride and a catalytic amount of triethylborane
AUTHOR(S): Kiyooka, S.-i.; Li, Y.-N.; Shahid, K. A.; Okazaki, M.; Shuto, Y.
CORPORATE SOURCE: Faculty of Science, Department of Chemistry, Kochi University, Kochi, 780-8520, Japan
SOURCE: Tetrahedron Letters (2001), 42(41), 7299-7301
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

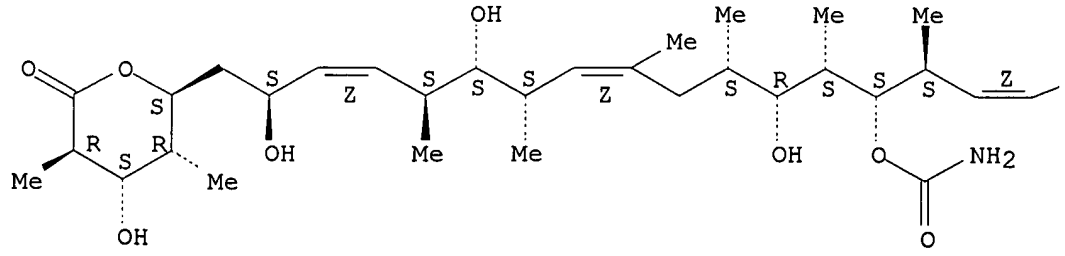
AB An interesting 2,4-syn dialkyl diastereoselection has been obsd. in the radical debromination of .alpha.-bromo-.alpha.-methyl-.delta.-valerolactones. The reaction of 4-alkyl-2-bromo-3-hydroxy-2-methyl-5-pentanolides with Bu3SnH and a catalytic amt. of Et3B gave, essentially, a single diastereomer with a 2,4-syn dialkyl relationship, independent of the orientation of the hydroxy substituent at C-3.

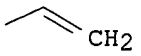
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(intermediate; diastereoselection in the radical debromination of bromomethylvalerolactones with tri-n-butyltin hydride and a catalytic amt. of triethylborane)

RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:686927 CAPLUS
DOCUMENT NUMBER: 136:95570
TITLE: The relationship between Taxol and (+)-discodermolide: synthetic analogs and modeling studies
AUTHOR(S): Martello, L. A.; LaMarche, M. J.; He, L.; Beauchamp, T. J.; Smith, A. B.; Horwitz, S. B.
CORPORATE SOURCE: Dep. Mol. Pharmacol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA
SOURCE: Chemistry & Biology (2001), 8(9), 843-855
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB During the past decade, Taxol has assumed an important role in cancer chemotherapy. The search for novel compds. with a mechanism of action similar to that of Taxol, but with greater efficacy particularly in Taxol-resistant cells, has led to the isolation of new natural products. One such compd., (+)-discodermolide, although structurally distinct from Taxol, has a similar ability to stabilize microtubules. In addn., (+)-discodermolide is active in Taxol-resistant cell lines that overexpress P-glycoprotein, the multidrug-resistant transporter. Interestingly, (+)-discodermolide demonstrates a profound enhancement of the initiation process of microtubule polymn. compared to Taxol. The synthesis of (+)-discodermolide analogs exploiting our highly efficient, triply convergent approach has permitted structure-activity relation (SAR) studies. Small changes to the (+)-discodermolide structure resulted in a dramatic decrease in the ability of all four discodermolide analogs to initiate tubulin polymn. Two of the analogs also demonstrated a decrease in total tubulin polymn., while a change in the olefin geometry at the C8 position produced a significant decrease in cytotoxic activity. The availability of (+)-discodermolide and the analogs, and the resultant SAR anal., have permitted an exploration of the similarities and differences between (+)-discodermolide and Taxol. Docking of the x-ray/soln. structure of (+)-discodermolide into the Taxol binding site of .beta.-tubulin revealed two possible binding modes (models I and II). The preferred pharmacophore model (I), in which the C19 side chain of (+)-discodermolide matches with the C2 benzoyl group of Taxol and the .delta.-lactone ring of (+)-discodermolide overlays with the C13 side chain of Taxol, concurred with the results of the SAR anal.

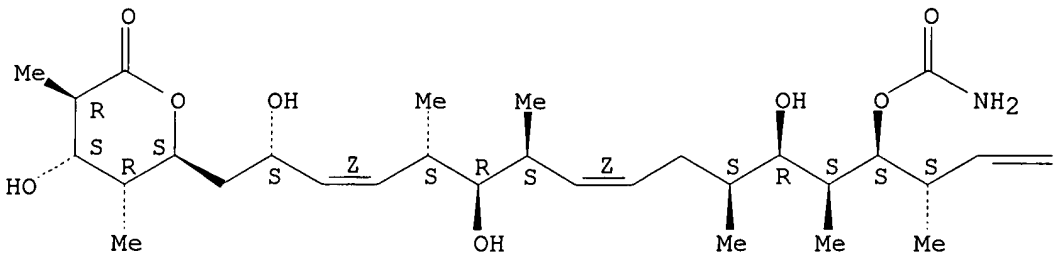
IT **127943-53-7**, (+)-Discodermolide **358968-14-6** **389056-34-2** **389056-35-3** **389056-36-4**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microtubule stabilizing structure activity relationships of Taxol and (+)-discodermolide analogs)

RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-

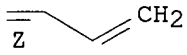
[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,11,13,15-pentamethyl-3,8,16,18-nonatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



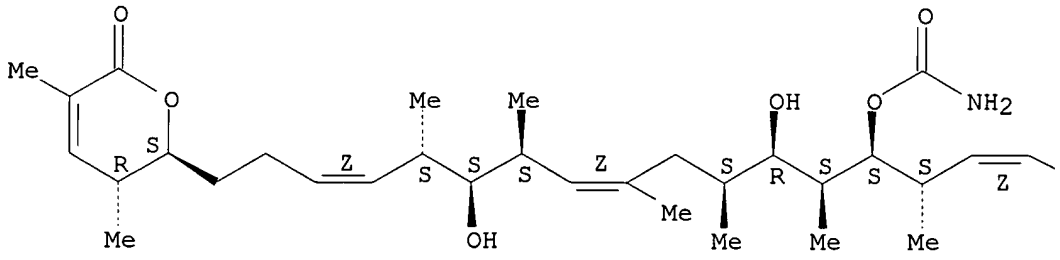
PAGE 1-B



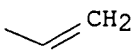
RN 389056-35-3 CAPLUS
CN 2H-Pyran-2-one, 6-[(3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



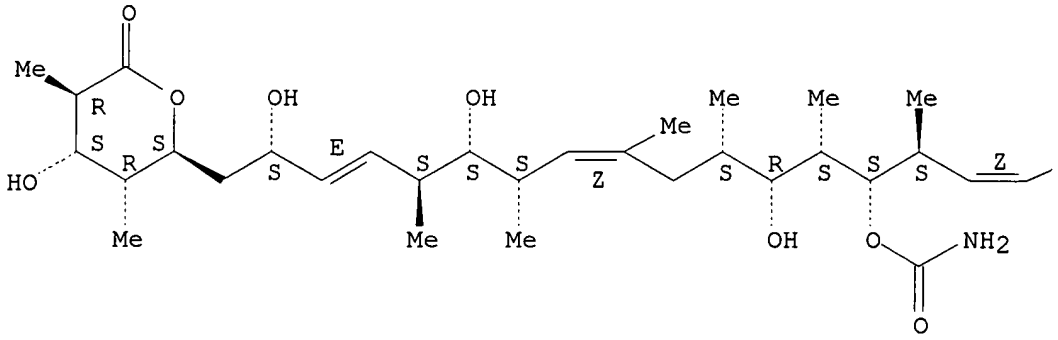
PAGE 1-B



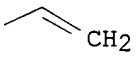
RN 389056-36-4 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3E,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:661409 CAPLUS
DOCUMENT NUMBER: 135:226827
TITLE: Biologically active analogs of discodermolide
INVENTOR(S): Gunasekera, Sarath P.; Longley, Ross E.; Isbrucker, Richard A.; Paul, Gopal K.; Pomponi, Shirley A.; Wright, Amy E.
PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution, Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064663	A2	20010907	WO 2001-US6367	20010228
WO 2001064663	A3	20020228		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001049387 A1 20011206 US 2001-796175 20010228
PRIORITY APPLN. INFO.: US 2000-186145P P 20000301
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The subject invention provides novel compns. of biol. active analogs of discodermolide (I), such as, 2-(desmethyl)discodermolide, 19-(desaminocarbonyl)discodermolide, 2-epidiscodermolide, Me discodermolate (II), 3-deoxy-2.DELTA.-discodermolide (III), 8,21,23-hexahydrodiscodermolide and 7-deoxy-8,21,23-hexahydrodiscodermolide (IV), which can advantageously be used for immunomodulation and/or treating cancer, have utility for use in the treatment of cancer, as tubulin polymerizers and as microtubule stabilization agents, and also pertains to the identification of regions of the discodermolide mol. which are responsible for certain aspects of the bioactivity of discodermolide compds. Thus, 3-deoxy-2.DELTA.-discodermolide (III) was prepd. from discodermolide 3-acetate via treatment with Na2CO3 in aq. EtOH. 3-Deoxy-2.DELTA.-discodermolide (III) was tested for antitumor activity [IC50 = 20 ng/mL vs. P388 cells; IC50 = 12.5 ng/mL vs. A549 cells; microtubule bundling in A549 cells = +++; purified tubulin polymn. at 10 .mu.M = +21.degree.; cell cycle effect = some apoptosis in G2/M block at 100 nM].

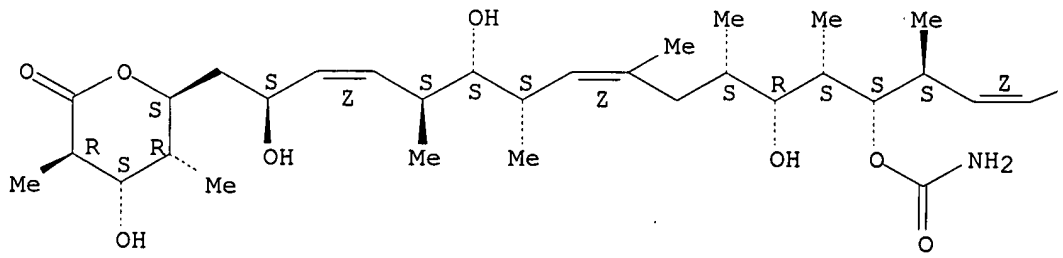
IT **127943-53-7DP**, Discodermolide, analogs
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)

RN 127943-53-7 CAPLUS

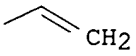
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



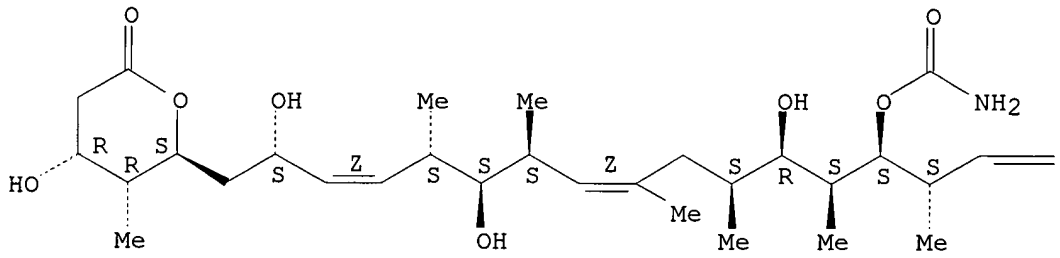
IT **358968-10-2**, 2-(Desmethyl)discodermolide **358968-11-3**, 19-(Desaminocarbonyl)discodermolide **358968-12-4** **358968-13-5**, Methyl discodermolate
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)

RN 358968-10-2 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-5-methyl-, (4R,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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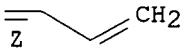
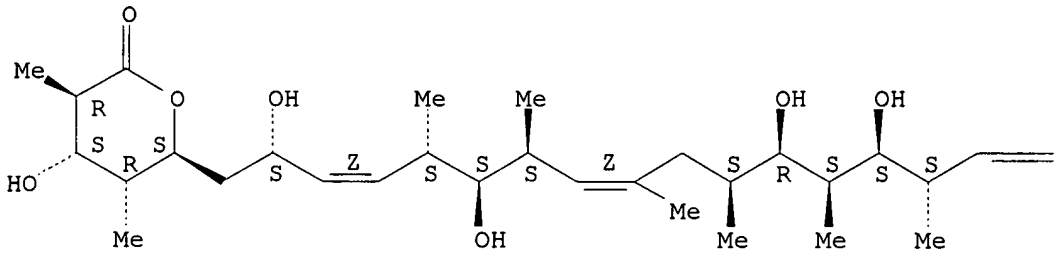


RN 358968-11-3 CAPLUS

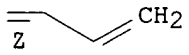
CN 2H-Pyran-2-one, tetrahydro-4-hydroxy-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12,14-tetrahydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



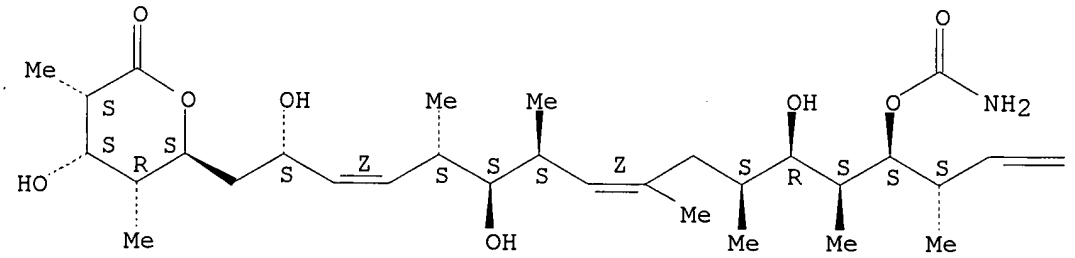
PAGE 1-B



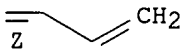
RN 358968-12-4 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



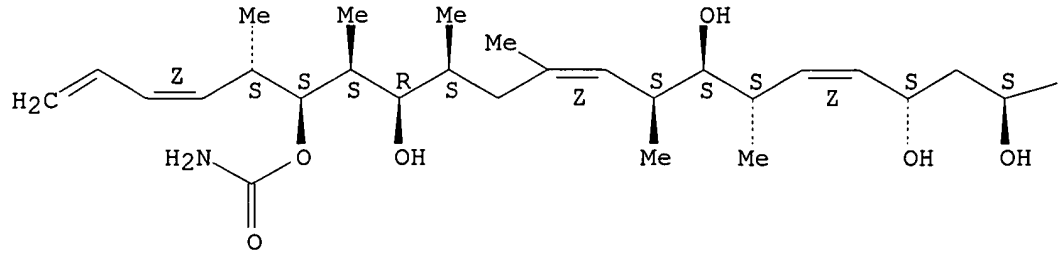
PAGE 1-B



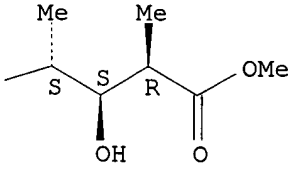
RN 358968-13-5 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,5,7,11,17-pentahydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4S,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



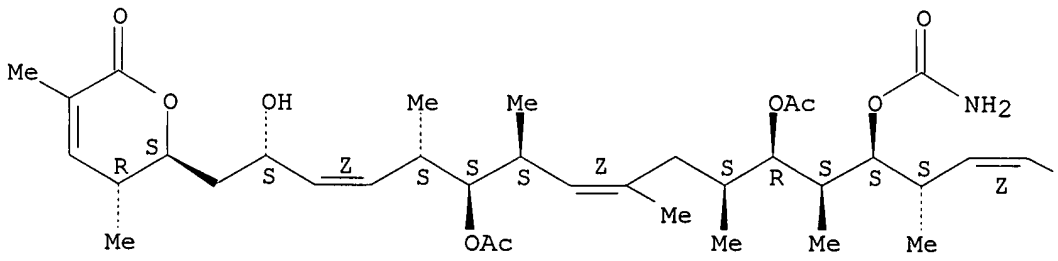
PAGE 1-B



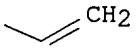
IT **358968-16-8P**, 3-Deoxy-2.DELTA.-discodermolide 11,17-diacetate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)
RN 358968-16-8 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-6,12-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-2-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



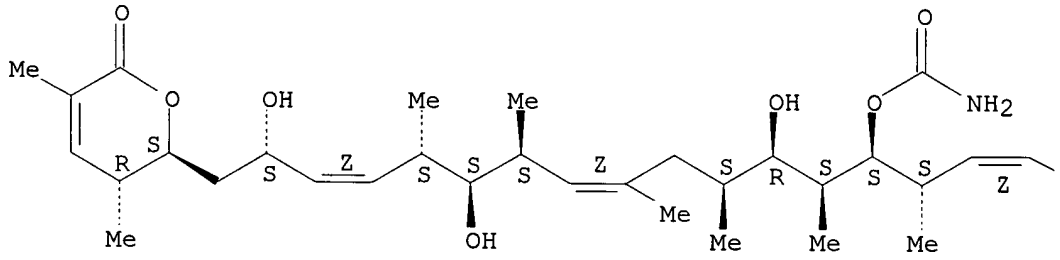
IT **358968-14-6P**, 3-Deoxy-2.DELTA.-discodermolide **358968-15-7P**, 3-Deoxy-2.DELTA.-discodermolide 17-acetate **358968-17-9P**, 3-Deoxy-2.DELTA.-discodermolide 7,11,17-triacetate **358968-29-3P**, 3-Deoxy-2.DELTA.-discodermolide 11-acetate **358968-30-6P**, 3-Deoxy-2.DELTA.-discodermolide 7-succinate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)

RN 358968-14-6 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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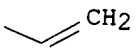
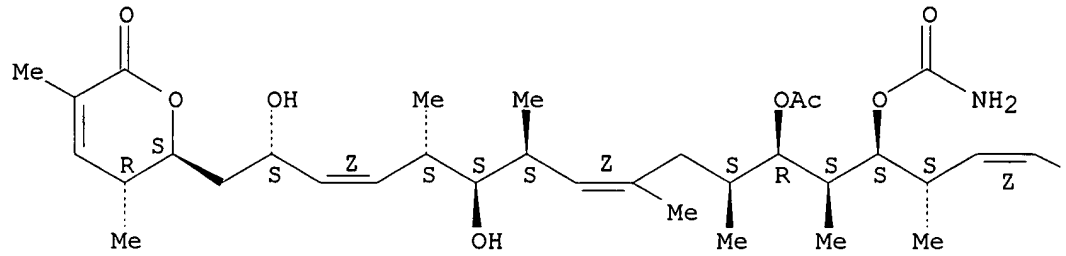


RN 358968-15-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-12-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,6-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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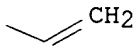
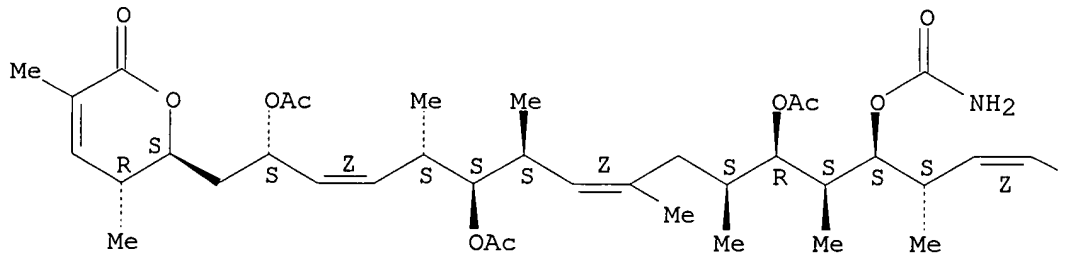


RN 358968-17-9 CAPLUS
CN 2H-Pyran-2-one, 5,6-dihydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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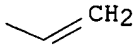
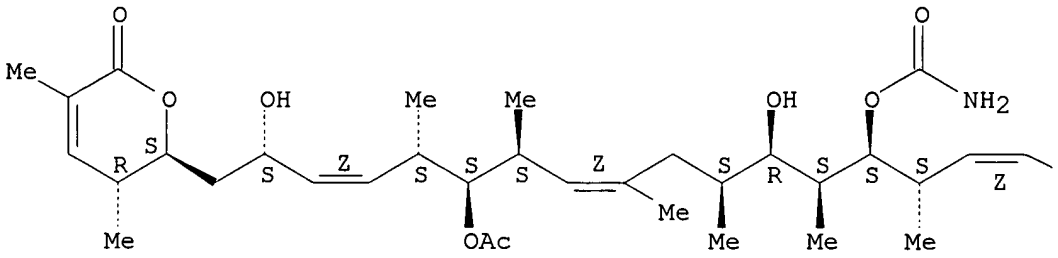


RN 358968-29-3 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-6-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-5,6-dihydro-3,5-dimethyl-, (5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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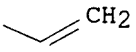
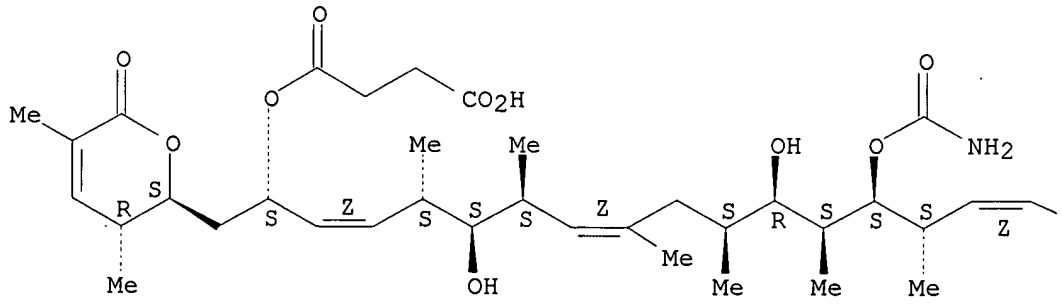


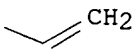
RN 358968-30-6 CAPLUS
CN Butanedioic acid, mono[(1S,2Z,4S,5S,6S,7Z,10S,11R,12S,13S,14S,15Z)-13-[(aminocarbonyl)oxy]-1-[[(2S,3R)-3,6-dihydro-3,5-dimethyl-6-oxo-2H-pyran-2-yl]methyl]-5,11-dihydroxy-4,6,8,10,12,14-hexamethyl-2,7,15,17-octadecatetraenyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



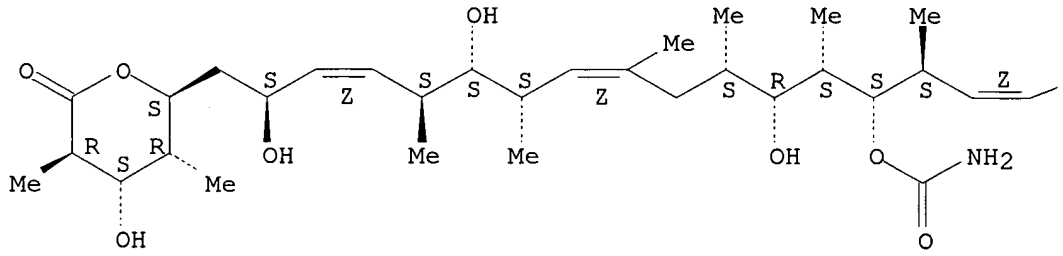
PAGE 1-B



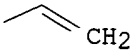
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



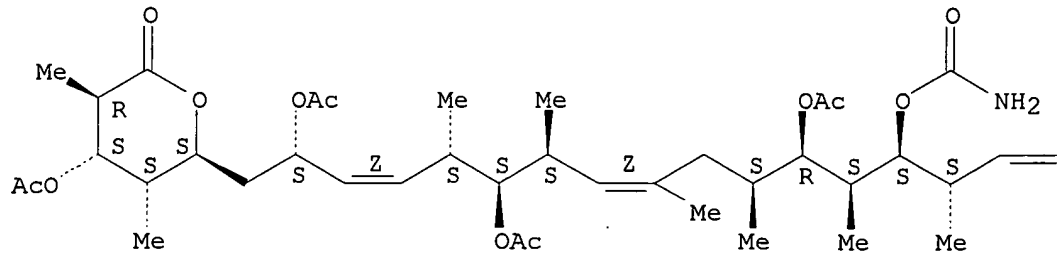
PAGE 1-B



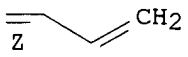
IT **299173-77-6**, Discodermolide 3,7,11,17-tetraacetate
299173-79-8, Discodermolide 3,7,11-triacetate **299173-83-4**
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. or isolation and anticancer activity of discodermolide analogs)
RN 299173-77-6 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



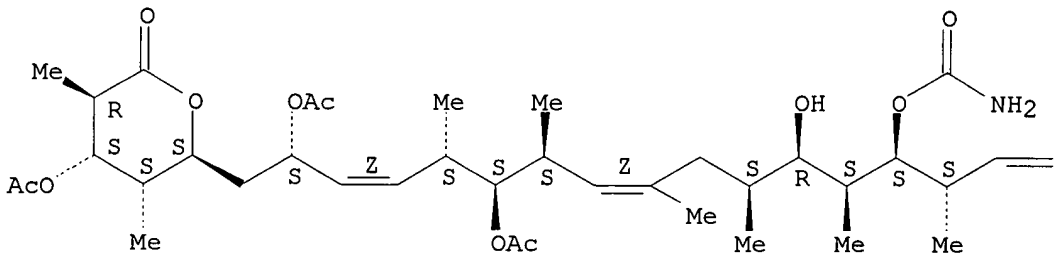
PAGE 1-B



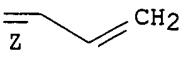
RN 299173-79-8 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



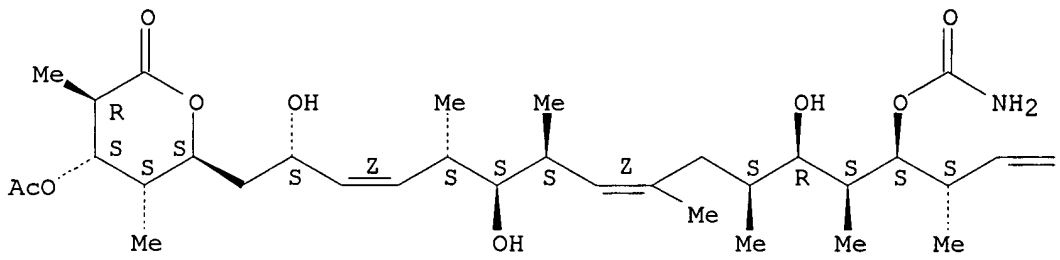
PAGE 1-B



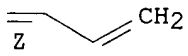
RN 299173-83-4 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 28 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:658077 CAPLUS
DOCUMENT NUMBER: 135:205580
TITLE: Method for inhibiting or treating chemotherapy-induced hair loss
INVENTOR(S): Atwal, Karnail S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. Ser. No. 447,002.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001020038	A1	20010906	US 2001-805347	20010313
US 6458835	B2	20021001		
US 6013668	A	20000111	US 1998-119884	19980721
ZA 9807220	A	20000214	ZA 1998-7220	19980812
US 6472427	B1	20021029	US 1999-447002	19991122
US 6262122	B1	20010717	US 2000-615345	20000712

PRIORITY APPLN. INFO.: US 1997-55568P P 19970813
US 1998-71364P P 19980115
US 1998-119884 A1 19980721
US 1999-447002 A2 19991122

AB A method for inhibiting hair loss and/or promoting hair growth in chemotherapy and/or radiation therapy patients wherein the (R)-enantiomer of 4-[[(cyanoimino)-[(1,2,2-trimethylpropyl)amino]methyl]amino]benzonitrile is administered prior to, simultaneous with and/or after chemotherapy and/or radiation treatment. There was a remarkable difference between the 1-(R)-enantiomer and the 2-(S)enantiomer in their effect on hair follicle

stimulation; in particular the (R)-enantiomer had a faster onset of action compared to the corresponding (S)-enantiomer. While the IC50 for vasorelaxant potency of the (R)-enantiomer is 47.+-.17 nM vs. 157.+-.35 nM for the (S)-enantiomer, the hair growth promoting ability of the (R)-enantiomer for producing hair growth within 11 days of treatment is 8 times greater than the corresponding (S)-enantiomer.

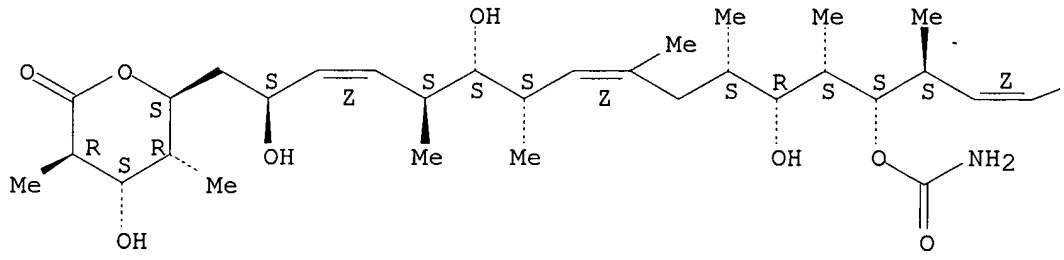
IT **127943-53-7**, Discodermolide
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor; method for inhibiting or treating chemotherapy-induced hair loss)

RN 127943-53-7 CAPLUS

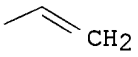
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 29 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:648827 CAPLUS
DOCUMENT NUMBER: 135:371555
TITLE: A Practical Synthesis of (+)-Discodermolide and Analogues: Fragment Union by Complex Aldol Reactions
AUTHOR(S): Paterson, Ian; Florence, Gordon J.; Gerlach, Kai; Scott, Jeremy P.; Sereinig, Natascha
CORPORATE SOURCE: University Chemical Laboratory, Cambridge University, Cambridge, CB2 1EW, UK
SOURCE: Journal of the American Chemical Society (2001), 123(39), 9535-9544
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:371555
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A practical stereocontrolled synthesis of (+)-discodermolide (I) has been completed in 10.3% overall yield (23 steps longest linear sequence). The abs. stereochem. of the C1-C6 (II; TBDMS = SiMe2CMe3, PMB = CH2C6H4OMe-4), C9-C16 (III), and C17-C24 (IV) subunits was established via substrate-controlled, boron-mediated, aldol reactions of the chiral Et ketones - (S)-PhCH2OCH2CHMeCOEt, (S)-4-MeOC6H4CH2OCH2CHMeCOEt, and (S)-EtCOCHMeO2CPh. Key fragment coupling reactions were a lithium-mediated, anti-selective, aldol reaction of aryl ester III (under Felkin-Anh induction from the aldehyde component IV), followed by in situ redn. to produce the 1,3-diol V, and a (+)-diisopinocampheylboron chloride-mediated aldol reaction of Me ketone II (overturning the inherent substrate induction from the aldehyde component VI) to give the (7S)-adduct VII. The flexibility of our overall strategy is illustrated by the synthesis of a no. of diastereomers and structural analogs of discodermolide, which should serve as valuable probes for structure-activity studies.

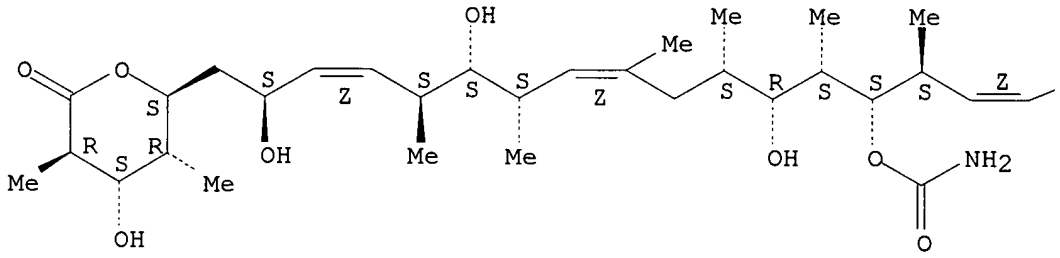
IT **127943-53-7P**, (+)-Discodermolide
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)

RN 127943-53-7 CAPLUS

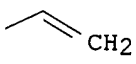
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



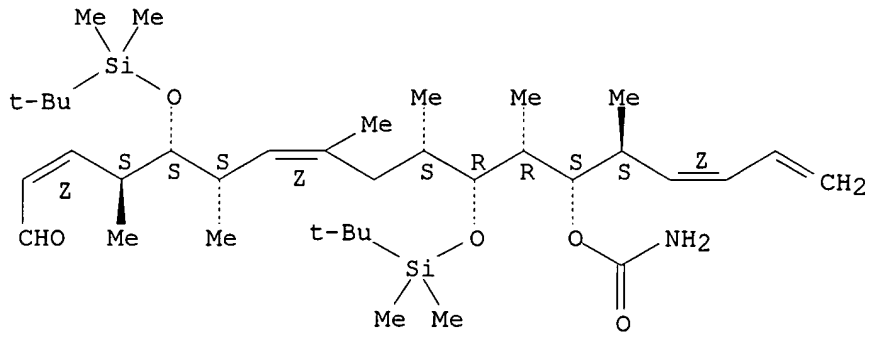
PAGE 1-B



IT **261968-08-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and boron-mediated aldol reaction of; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)

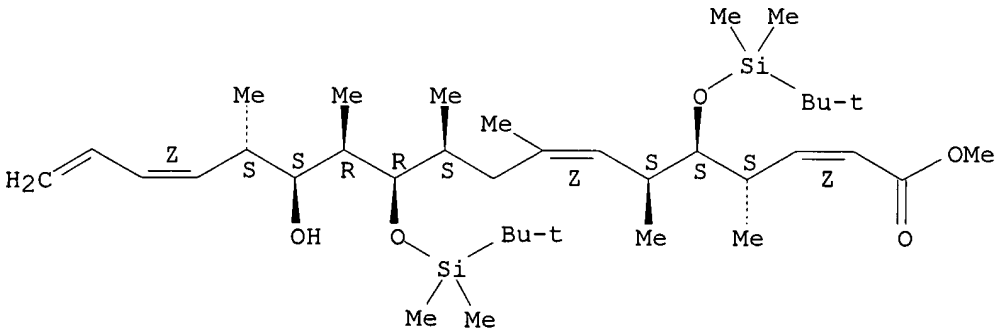
RN 261968-08-5 CAPLUS
CN 2,7,15,17-Octadecatetraenal, 13-[(aminocarbonyl)oxy]-5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **261968-24-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and carbamoylation of; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)
RN 261968-24-5 CAPLUS
CN 2,7,15,17-Octadecatetraenoic acid, 5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-hydroxy-4,6,8,10,12,14-hexamethyl-, methyl ester, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

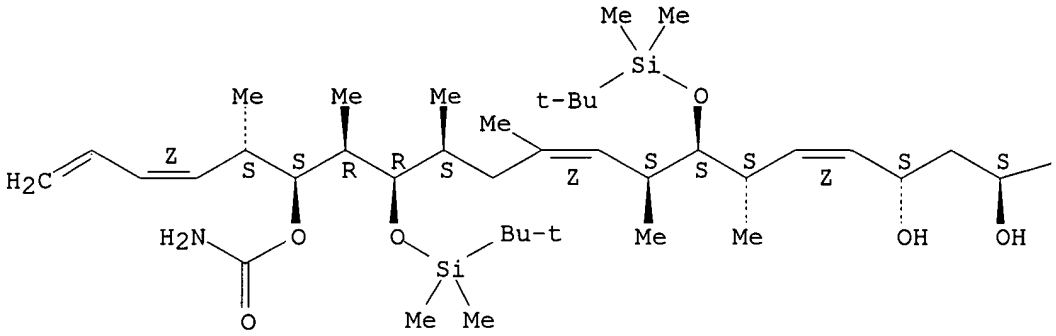


IT **261968-26-7P 373645-75-1P 373645-76-2P 373645-77-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and deprotection-lactonization to discodermolide; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)
RN 261968-26-7 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester,

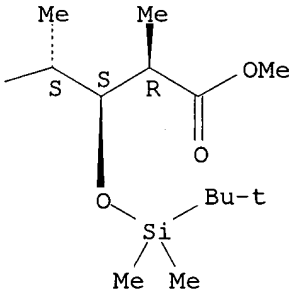
(2R,3S,4S,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



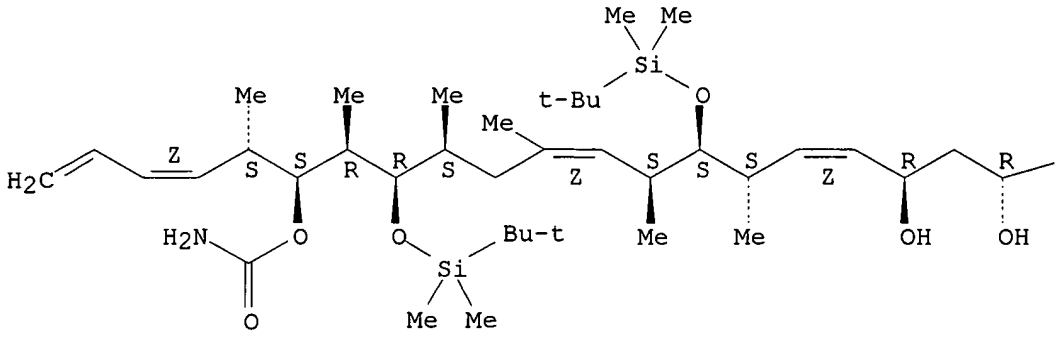
PAGE 1-B



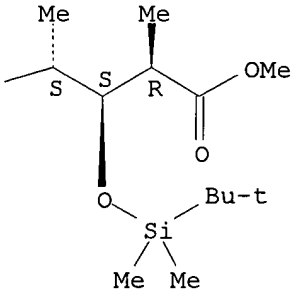
RN 373645-75-1 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4S,5R,7R,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



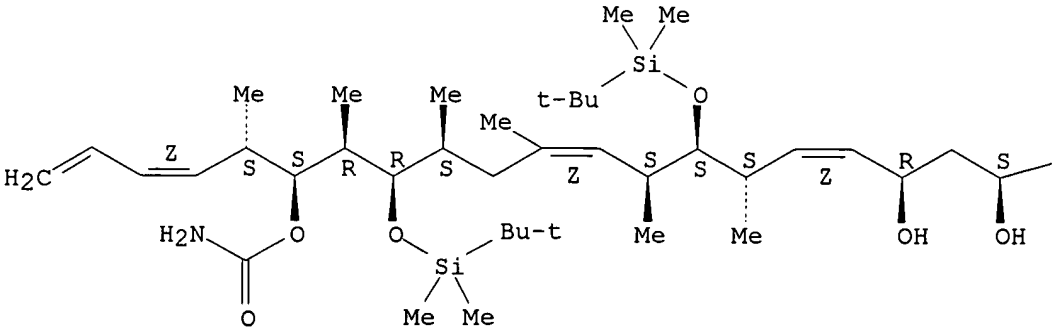
PAGE 1-B



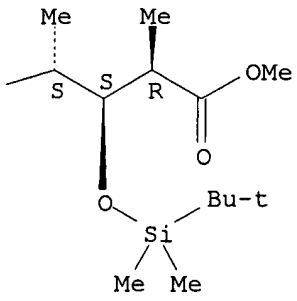
RN 373645-76-2 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4S,5S,7R,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



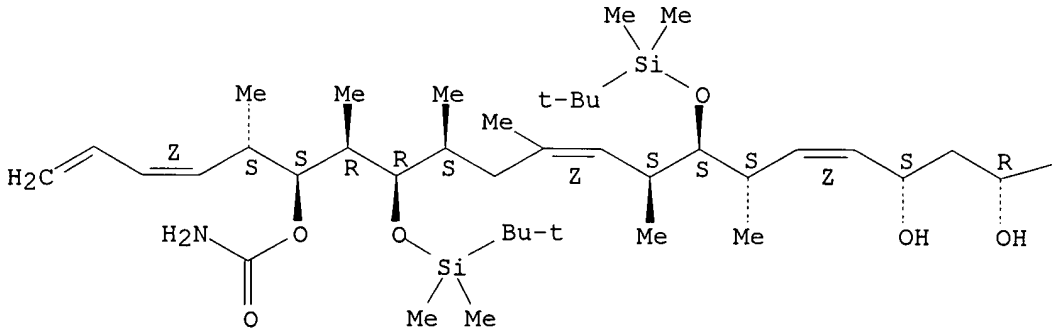
PAGE 1-B

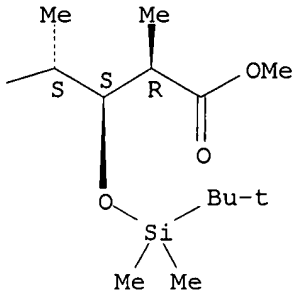


RN 373645-77-3 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4S,5R,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

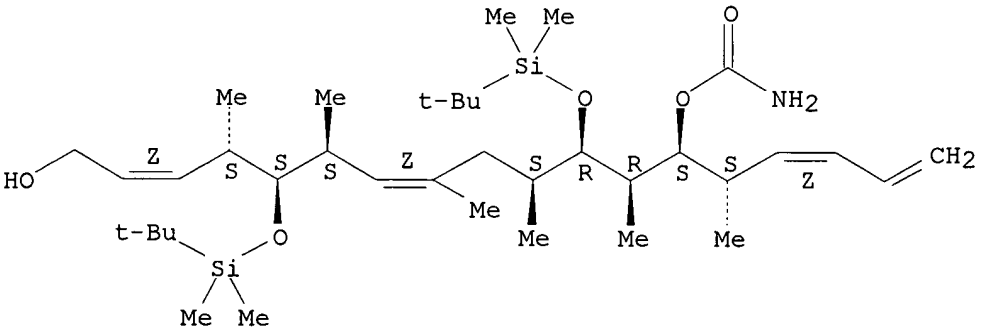
PAGE 1-A





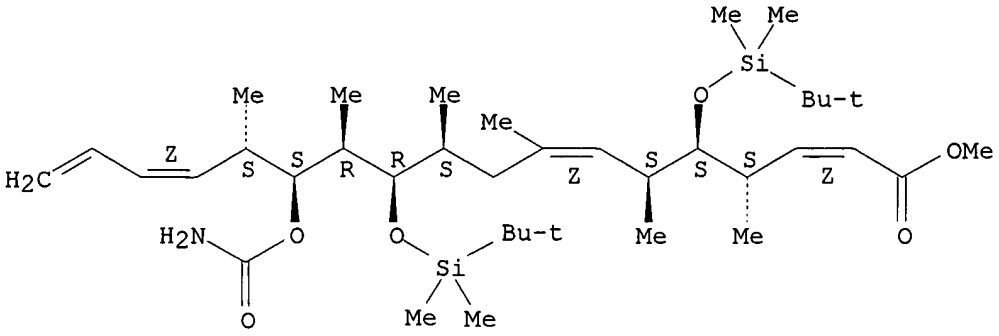
IT **373645-74-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and desilylation or Dess-Martin oxidn. of; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)
RN 373645-74-0 CAPLUS
CN 2,7,15,17-Octadecatetraene-1,13-diol, 5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, 13-carbamate, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



IT **373645-73-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)
RN 373645-73-9 CAPLUS
CN 2,7,15,17-Octadecatetraenoic acid, 13-[(aminocarbonyl)oxy]-5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, methyl ester, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



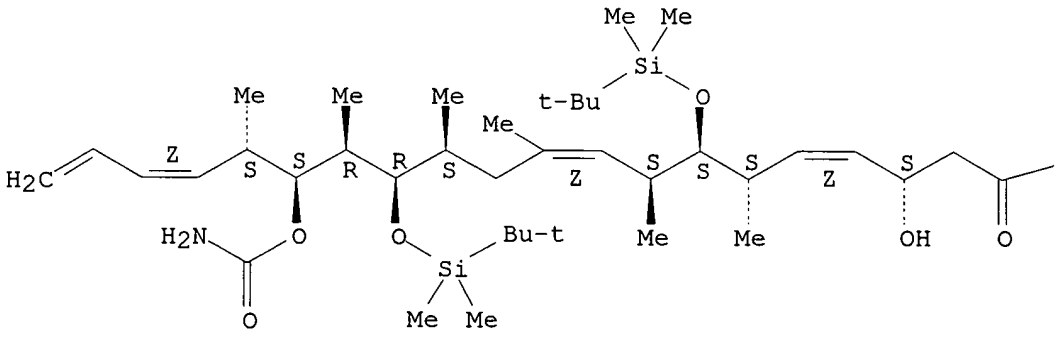
IT **261968-25-6P 303964-32-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and stereoselective boron-mediated aldols of; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)

RN 261968-25-6 CAPLUS

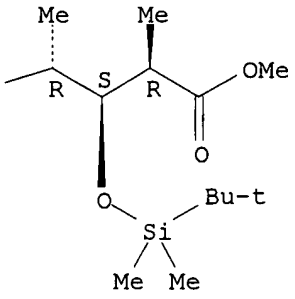
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-5-oxo-, methyl ester, (2R,3S,4R,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



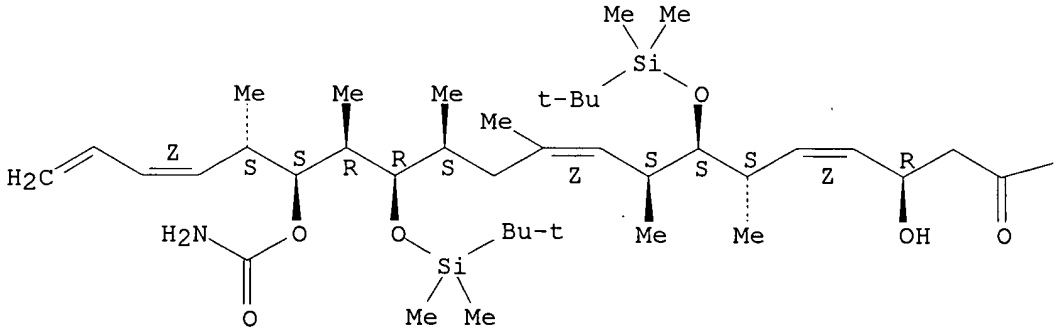
PAGE 1-B



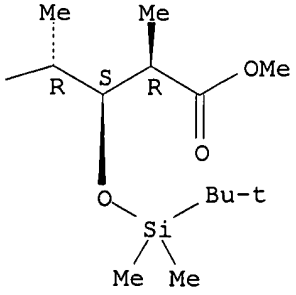
RN 303964-32-1 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-5-oxo-, methyl ester, (2R,3S,4R,7R,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



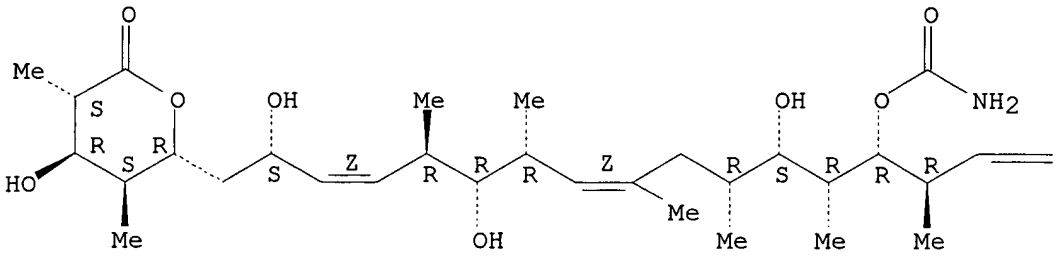
IT **194232-29-6P**, (+)-7-epi-Discodermolide **303964-33-2P**, 5-epi-Discodermolide **303964-35-4P**, 5,7-Di-epi-discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of as a potential cancer chemotherapeutic; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)

RN 194232-29-6 CAPLUS

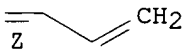
CN 2H-Pyran-2-one, 6-[(2S,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

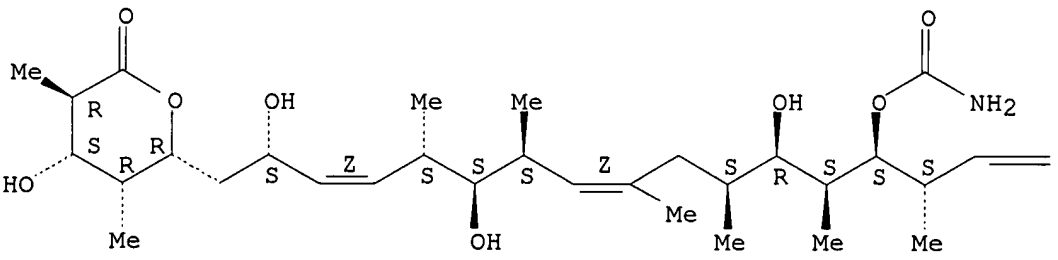


RN 303964-33-2 CAPLUS

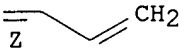
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



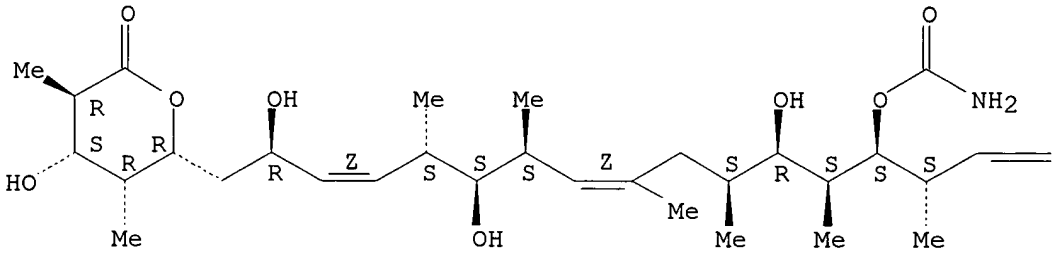
PAGE 1-B



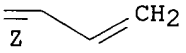
RN 303964-35-4 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

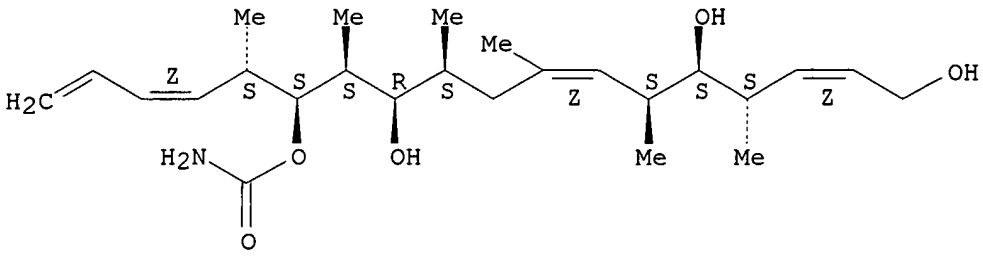


PAGE 1-B



IT **373645-78-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of as potential tubulin binding agent; boron-mediated aldol reaction route to the stereocontrolled synthesis of (+)-discodermolide and analogs)
RN 373645-78-4 CAPLUS
CN 2,7,15,17-Octadecatetraene-1,5,11,13-tetrol, 4,6,8,10,12,14-hexamethyl-, 13-carbamate, (2Z,4S,5S,6S,7Z,10S,11R,12S,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



REFERENCE COUNT: 107 THERE ARE 107 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:623506 CAPLUS
DOCUMENT NUMBER: 135:366201
TITLE: The epothilones, eleutherobins, and related types of molecules
AUTHOR(S): Stachel, Shawn J.; Biswas, Kaustav; Danishefsky, Samuel J.
CORPORATE SOURCE: The Laboratory for Bioorganic Chemistry, The Sloan-Kettering Institute for Cancer Research, New York, NY, 10021, USA
SOURCE: Current Pharmaceutical Design (2001), 7(13), 1277-1290
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

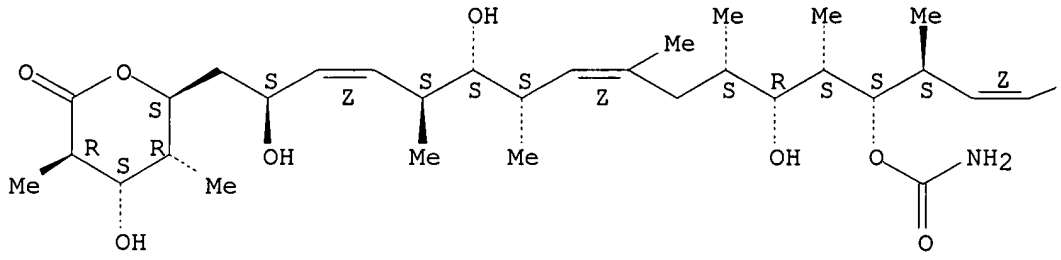
AB A review with refs. Taxol is currently one of the most effective anticancer agents available. However, limitations due to multidrug-resistance (MDR) susceptibility and lack of aq. soly. render it less than an ideal drug. These limitations, coupled with taxol's unique mechanism of tumor inhibition, involving the stabilization of microtubule assembly, have spurred the search for more effective chemotherapeutic agents. This review will discuss the chem. and biol. of some of the most promising new mols. with "taxol-like" activity. The extended family of microtubule-stabilizing agents now includes the epothilones, eleutherobins, discodermolide, laulimalide and WS9885B. The epothilones have emerged as one of the most exciting new candidates for detailed structure-activity-related studies. A review of our efforts in the synthetic and biol. aspects of this research is presented, as are the latest developments reported from other labs. in academia and the pharmaceutical industry. The synthesis and structure-activity studies of eleutherobins, as well as recent progress with discodermolide, laulimalide and WS9885B are also reviewed. An abundance of exciting advances in chem. and biol. have emerged from these studies, and it is hoped that it will ultimately result in the development of new and more effective chemotherapeutic agents in the fight against cancer.

IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor epothilones, eleutherobins, and related types of mols.)

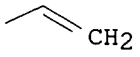
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:552436 CAPLUS
DOCUMENT NUMBER: 135:352420
TITLE: Selective potentiation of paclitaxel (Taxol)-induced cell death by mitogen-activated protein kinase kinase inhibition in human cancer cell lines
AUTHOR(S): McDaid, Hayley M.; Horwitz, Susan Band
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, USA
SOURCE: Molecular Pharmacology (2001), 60(2), 290-301
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation of the mitogen-activated protein kinase (MAPK) pathway in HeLa and Chinese hamster ovary cells after treatment with paclitaxel (Taxol) and other microtubule interacting agents has been investigated. Using a trans-reporting system, the phosphorylation of the nuclear transcription factors Elk-1 and c-jun was measured. Concn.- and time-dependent activation of the Elk-1 pathway, mediated primarily by the extracellular signal-regulated kinase (ERK) component of the MAPK family, was obsd. Inactive drug analogs and other cytotoxic compds. that do not target microtubules failed to induce similar levels of activation, thereby indicating that an interaction between these drugs and the microtubule is essential for the activation of MAPKs. Evaluation of the endogenous levels of MAPK expression revealed cell-dependent expression of the ERK, c-jun N-terminal kinase, and p38 pathways. In the case of HeLa cells, time-dependent activation of ERK coincided with increased poly(ADP-ribose) polymerase (PARP) cleavage, phosphatidylserine externalization, and increased accumulation of cells in G2M. In both cell lines, inhibition of ERK activity potentiated paclitaxel-induced PARP cleavage and phosphatidylserine externalization, suggesting that ERK activity coincided

with, but did not mediate, the cytotoxic effects of paclitaxel. We evaluated the nature of the interaction between paclitaxel and the MAPK kinase inhibitor U0126 in three cell lines, on the basis of a potential chemotherapeutic advantage of paclitaxel plus ERK inhibition. Our data confirmed additivity in those cells lines that undergo paclitaxel-induced ERK activation, and antagonism in cells with low ERK activity, suggesting that in tumors with high ERK activity, there may be an application for this strategy in therapy.

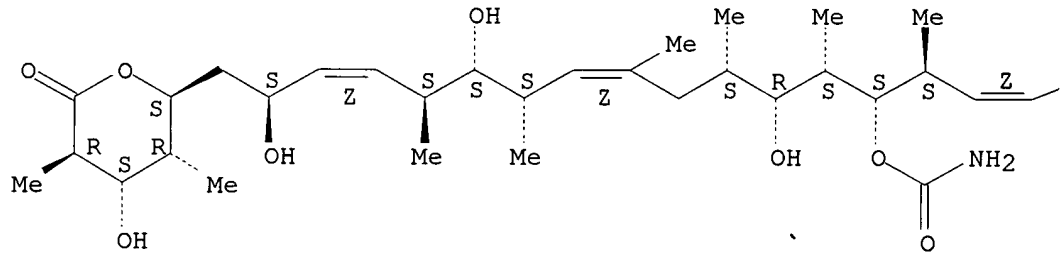
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of paclitaxel and other microtubule interacting substances on the MAPK pathway in human cancer cell lines)

RN 127943-53-7 CAPLUS

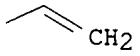
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

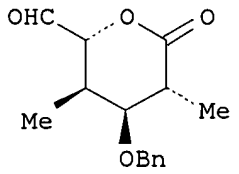


PAGE 1-B



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:538822 CAPLUS
DOCUMENT NUMBER: 135:303712
TITLE: Synthesis of the C1-C6 subunit of discodermolide from furan
AUTHOR(S): Arjona, O.; Menchaca, R.; Plumet, J.
CORPORATE SOURCE: Facultad de Quimica, Departamento de Quimica Organica I, Universidad Complutense, Madrid, 28040, Spain
SOURCE: Tetrahedron (2001), 57(31), 6751-6755
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The synthesis of the C1-C6 subunit (I) of the potent antitumor agent discodermolide has been performed using 7-oxanorbornene derivs., derived from furan, as key intermediates to control the stereochem. of the incoming functional groups.

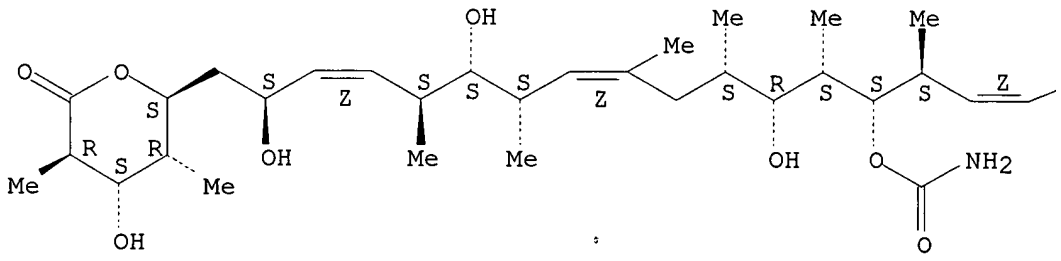
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of the C1-C6 subunit of discodermolide from furan)

RN 127943-53-7 CAPLUS

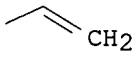
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



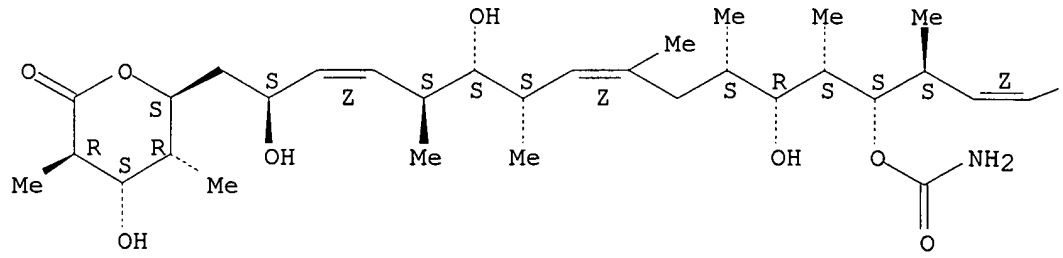
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:496203 CAPLUS
DOCUMENT NUMBER: 136:200041
TITLE: Detailed studies of fluorous tin compounds and combinatorial approach to the synthesis of discodermolide analogs
AUTHOR(S): Kim, Sun-Young
CORPORATE SOURCE: Univ. of Pittsburgh, Pittsburgh, PA, USA
SOURCE: (2000) 193 pp. Avail.: UMI, Order No. DA9984977
From: Diss. Abstr. Int., B 2001, 61(9), 4726
DOCUMENT TYPE: Dissertation

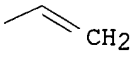
LANGUAGE: English
AB Unavailable
IT **127943-53-7DP**, Discodermolide, analogs
RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP (Preparation)
(combinatorial approach to the synthesis of discodermolide analogs using fluorinated tin reagents)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 34 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:495125 CAPLUS
DOCUMENT NUMBER: 136:334726
TITLE: Structure-activity relationship studies of discodermolide and its semisynthetic acetylated analogs on microtubule function and cytotoxicity
AUTHOR(S): Isbrucker, Richard A.; Gunasekera, Sarath P.; Longley, Ross E.
CORPORATE SOURCE: Division of Biomedical Marine Research, Harbor Branch Oceanographic Institution, Fort Pierce, FL, 34946, USA
SOURCE: Cancer Chemotherapy and Pharmacology (2001), 48(1), 29-36
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Discodermolide, a natural product from the marine sponge Discodermia dissoluta, has been previously described as an antimitotic agent with microtubule hyperstabilizing properties similar to those of paclitaxel (Taxol). The clin. success of paclitaxel has led to a growing interest in novel antimitotic compds. and the elucidation of their structure-activity characteristics. Analogs of discodermolide were prepd. by acetylation of the hydroxyl groups at carbons 3, 7, 11 and/or 17 and tested for biol.

activity in human tumor cells to det. the structural requirements for tubulin interaction and cytotoxic effects. A549 human lung adenocarcinoma cells were incubated with discodermolide, or its acetylated analogs, and examd. for their effects on microtubule architecture, cytotoxicity, and perturbations of the cell cycle. To confirm their direct interaction with tubulin, analogs were assayed for their ability to induce the polymn. of purified bovine brain tubulin. Acetylation of discodermolide at the C-7 hydroxyl group potentiated the cytotoxicity of the mol. to A549 cells, whereas acetylation at the C-3 hydroxyl group had little effect on the cytotoxicity of the parent or C-7-acetylated compds. The acetylation of the hydroxyl groups at the C-11 and C-17 positions severely abrogated the cytotoxicity of the mol. Cell cycle anal. by flow cytometry revealed that the more cytotoxic analogs caused the accumulation of cells in the G2/M phase, a mechanism previously reported for discodermolide. All discodermolide analogs with IC50 values below 1000 nM exhibited microtubule effects to varying degrees in cultured A549 cells, yet only the most cytotoxic promoted the polymn. of purified tubulin. Although the parent compd. was more effective at polymg. purified tubulin, acetylation of the C-3 or C-3 and C-7 hydroxyl groups improved its cytotoxicity in whole cells suggesting that acetylation either enhances accumulation of the mols. within cells or imparts a secondary cytotoxic quality not present in the discodermolide mol. The study reported here is the first to provide information on the structure-activity relationships of discodermolide using human tumor cells and analogs produced by semisynthetic modification of natural discodermolide.

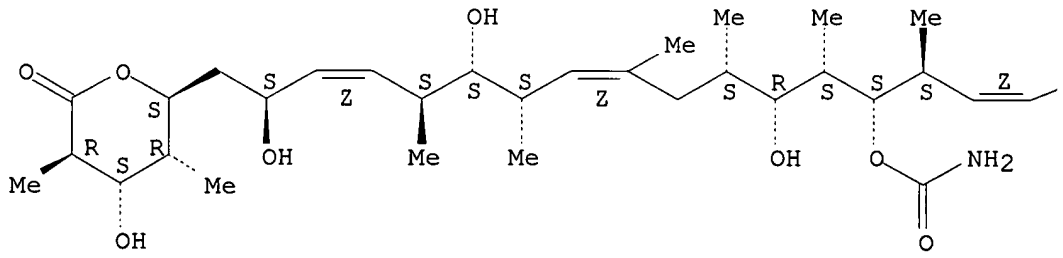
IT **127943-53-7**, Discodermolide
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(structure-activity relationship studies of discodermolide and its semisynthetic acetylated analogs on microtubule function and cytotoxicity)

RN 127943-53-7 CAPLUS

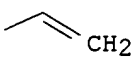
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



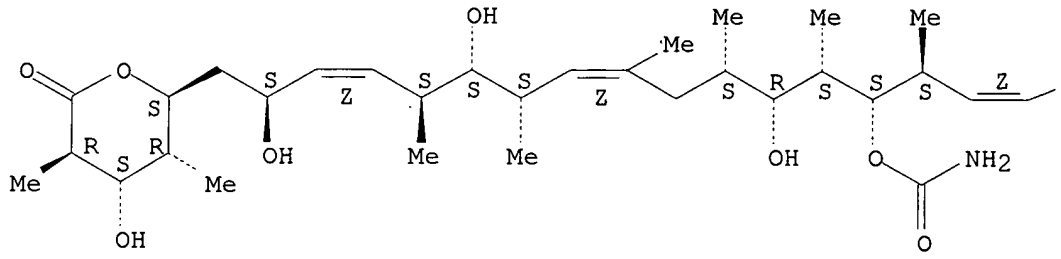
IT **127943-53-7DP**, Discodermolide, acetylated analogs
299173-77-6P, Discodermolide-3,7,11,17-tetraacetate
299173-78-7P 299173-79-8P, Discodermolide-3,7,11-triacetate **299173-80-1P**, Discodermolide-3,7-diacetate
299173-81-2P, Discodermolide-3,11-diacetate **299173-82-3P**, Discodermolide-3,17-diacetate **299173-83-4P**, Discodermolide-3-acetate **299173-84-5P**, Discodermolide-7-acetate
RL: PAC (Pharmacological activity); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationship studies of discodermolide and its semisynthetic acetylated analogs on microtubule function and cytotoxicity)

RN 127943-53-7 CAPLUS

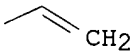
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

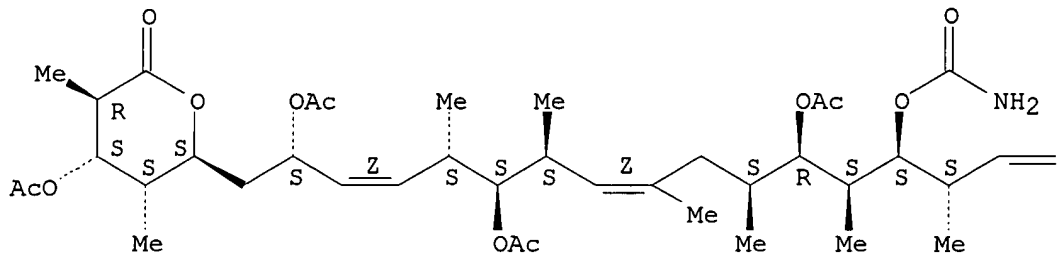


RN 299173-77-6 CAPLUS

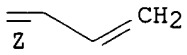
CN 2H-Pyran-2-one, 4-(acetyloxy)tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



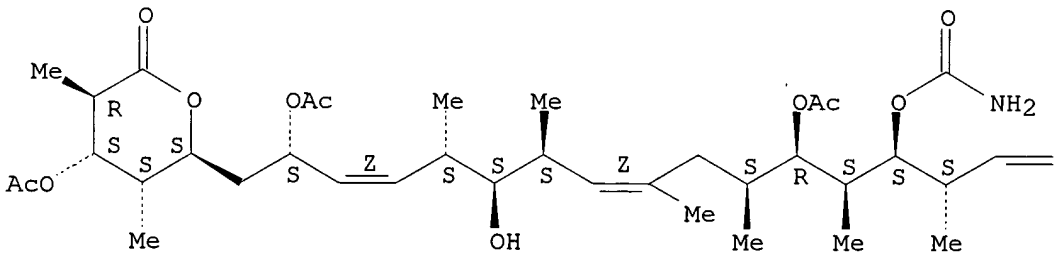
PAGE 1-B



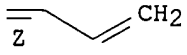
RN 299173-78-7 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,12-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-6-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



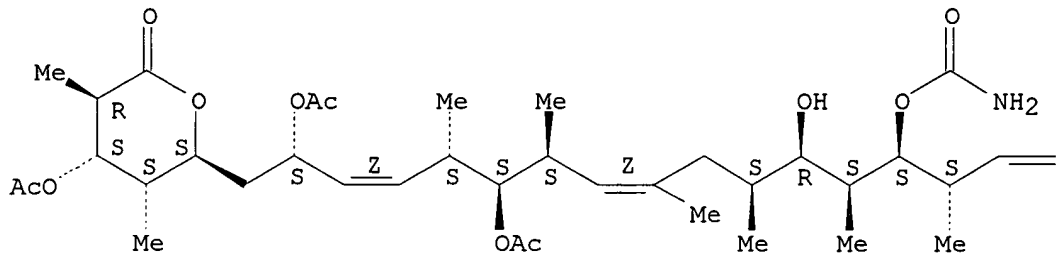
PAGE 1-B



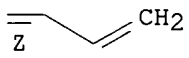
RN 299173-79-8 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



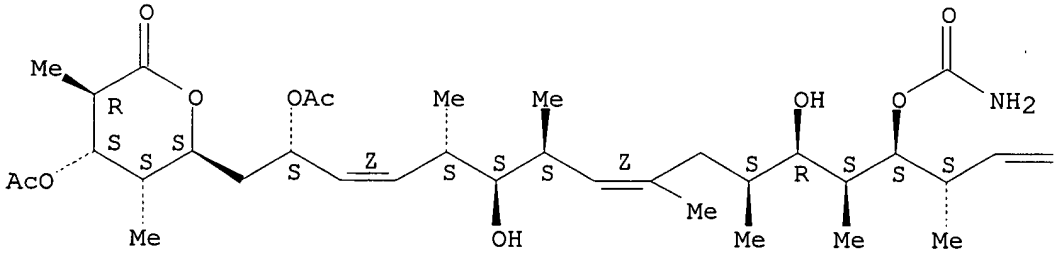
PAGE 1-B



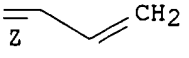
RN 299173-80-1 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

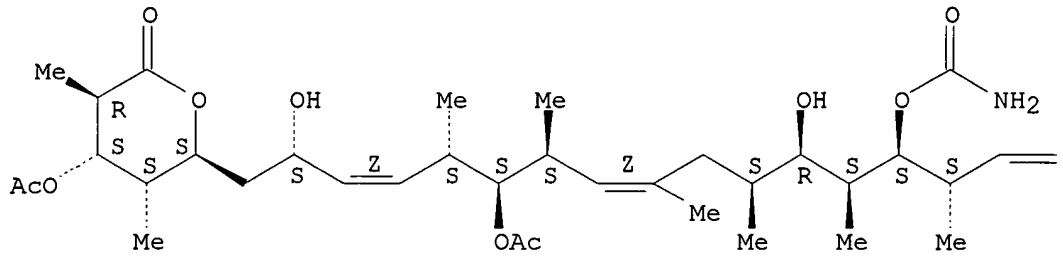


RN 299173-81-2 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16

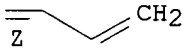
Z)-6-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



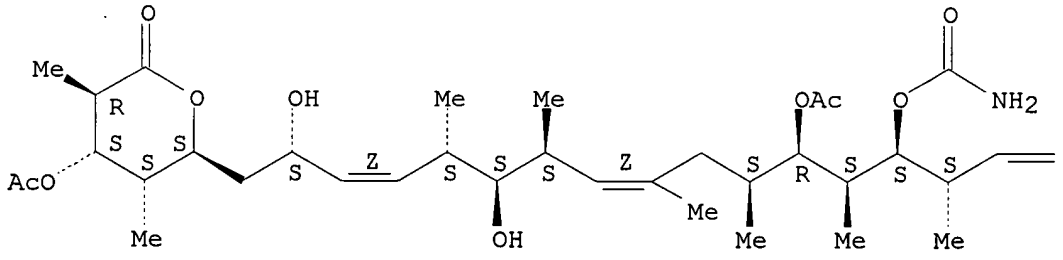
PAGE 1-B



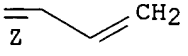
RN 299173-82-3 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-12-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,6-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



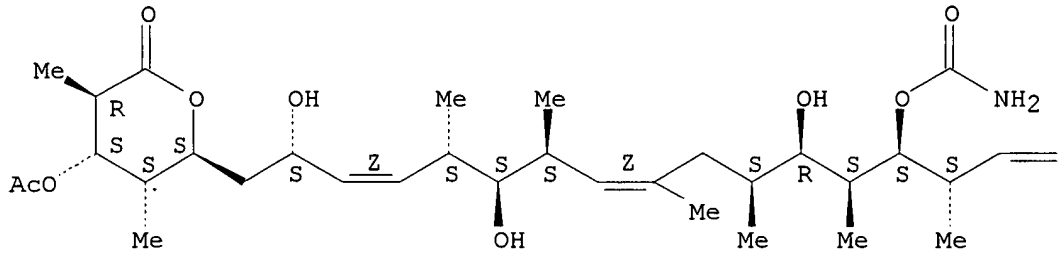
PAGE 1-B



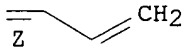
RN 299173-83-4 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



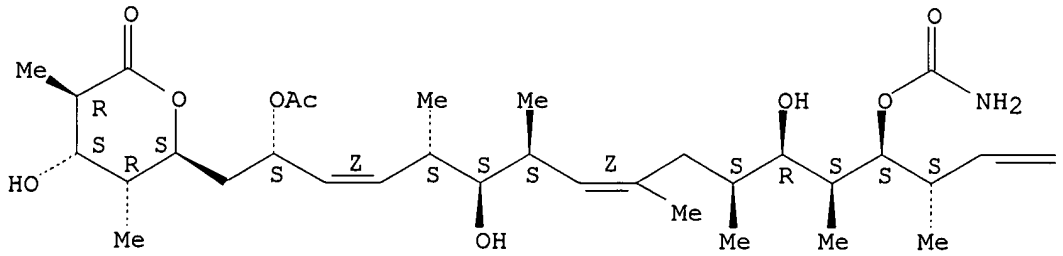
PAGE 1-B

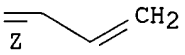


RN 299173-84-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

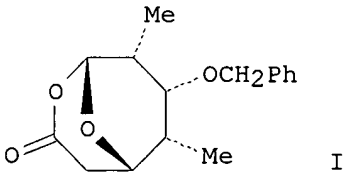
PAGE 1-A





REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:457114 CAPLUS
DOCUMENT NUMBER: 135:242050
TITLE: Towards the synthesis of (+)-discodermolide
AUTHOR(S): Yadav, J. S.; Abraham, S.; Reddy, M. M.; Sabitha, G.; Sankar, A. R.; Kunwar, A. C.
CORPORATE SOURCE: Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India
SOURCE: Tetrahedron Letters (2001), 42(28), 4713-4716
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:242050
GI



I

AB An approach to the asym. synthesis of fragments corresponding to C1-C7 and C15-C24 of (+)-discodermolide was reported. Key elements of the successful strategy include elaboration of two advanced fragments from a common precursor I obtained from Baeyer-Villiger oxidn.

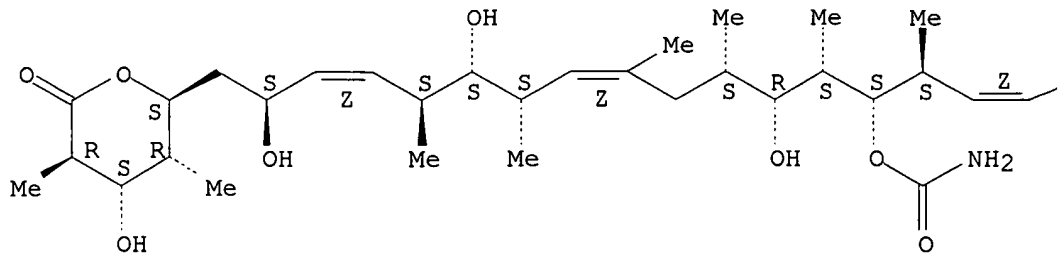
IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(towards the synthesis of (+)-discodermolide)

RN 127943-53-7 CAPLUS

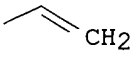
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:442810 CAPLUS
DOCUMENT NUMBER: 135:195442
TITLE: The Conformations of Discodermolide in DMSO
AUTHOR(S): Monteagudo, Edith; Cicero, Daniel O.; Cornett, Ben; Myles, David C.; Snyder, James P.
CORPORATE SOURCE: Universidad Nacional de Quilmes, Buenos Aires, 1876, Argent.
SOURCE: Journal of the American Chemical Society (2001), 123(28), 6929-6930
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

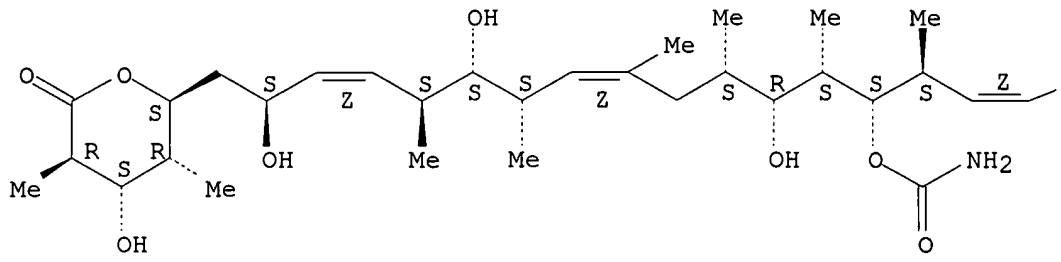
AB Conformations of discodermolide in DMSO is measured by NMR and single-crystal X-ray structure (no data) and falls into the corkscrew family.

IT **127943-53-7**, Discodermolide
RL: PRP (Properties)
(conformations of discodermolide in DMSO)

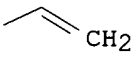
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

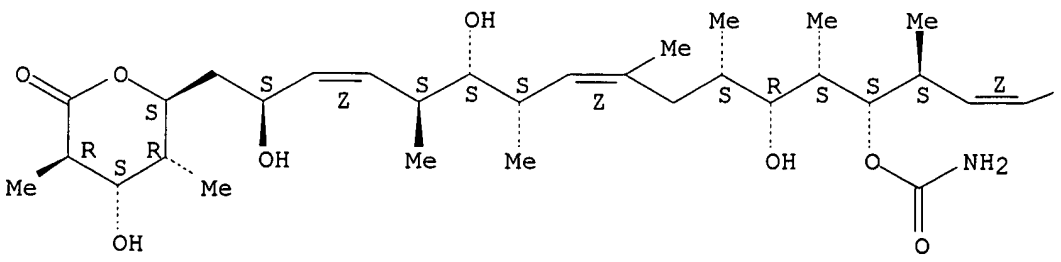


REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

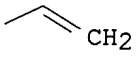
L4 ANSWER 37 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:438966 CAPLUS
DOCUMENT NUMBER: 135:180656
TITLE: Syntheses of (+)-discodermolide, nordiscodermolides, and the C1 to C11 fragment of tedanolide
AUTHOR(S): Lee, Christopher P.
CORPORATE SOURCE: Univ. of California, Los Angeles, CA, USA
SOURCE: (2000) 270 pp. Avail.: UMI, Order No. DA9986819
From: Diss. Abstr. Int., B 2001, 61(9), 4735
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7P**, (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of discodermolide and nordiscodermolides and fragments of tedanolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



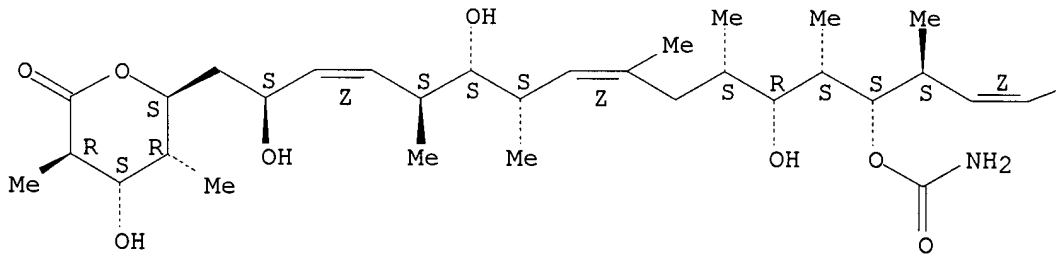
PAGE 1-B



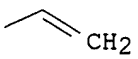
L4 ANSWER 38 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:438412 CAPLUS
DOCUMENT NUMBER: 135:174671
TITLE: Development of a common pharmacophore model for taxol and the epothilones
AUTHOR(S): He, Lifeng
CORPORATE SOURCE: Yeshiva Univ., New York, NY, USA
SOURCE: (2000) 128 pp. Avail.: UMI, Order No. DA9985216
From: Diss. Abstr. Int., B 2001, 61(9), 4663
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of a common pharmacophore model for taxol and epothilones)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 39 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:412961 CAPLUS

DOCUMENT NUMBER: 135:166711
TITLE: Asymmetric aldol reactions using boron enolates: applications to polyketide synthesis
AUTHOR(S): Paterson, Ian; Doughty, Victoria A.; Florence, Gordon; Gerlach, Kai; McLeod, Malcolm D.; Scott, Jeremy P.; Trieselmann, Thomas
CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK
SOURCE: ACS Symposium Series (2001), 783(Organoboranes for Syntheses), 195-206
CODEN: ACSMC8; ISSN: 0097-6156
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

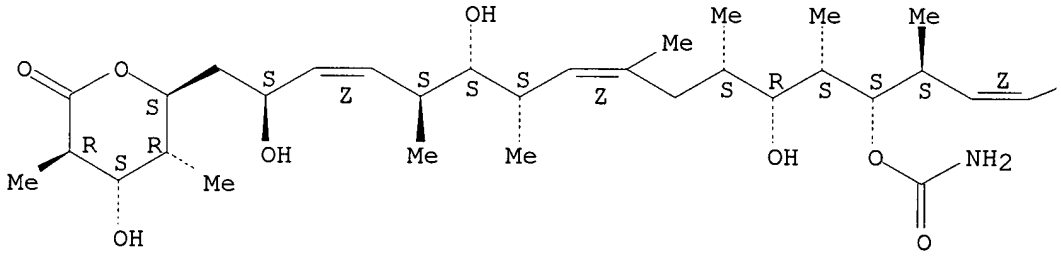
AB A review with 56 refs., chiral boron enolates add to aldehydes with high levels of stereocontrol in a predictable sense. These enolates are designed specifically for the aldol-based construction of the highly oxygenated and stereochem. challenging structures found in polyketide natural products, as illustrated here by their application to the total synthesis of concanamycin F and discodermolide.

IT **127943-53-7P**, Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. aldol reactions using boron enolates, applications to polyketide synthesis)

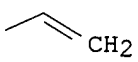
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:412212 CAPLUS
DOCUMENT NUMBER: 135:19496
TITLE: Preparation of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone

derivatives for pharmaceutical use

INVENTOR(S): Smith, Iii Amos B.; Beauchamp, Thomas J.; Lamarche, Matthew J.; Arimoto, Hirokazu

PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA

SOURCE: U.S., 126 pp., 6096904 Cont.-in-part of U.S. 6,096,904.
CODEN: USXXAM

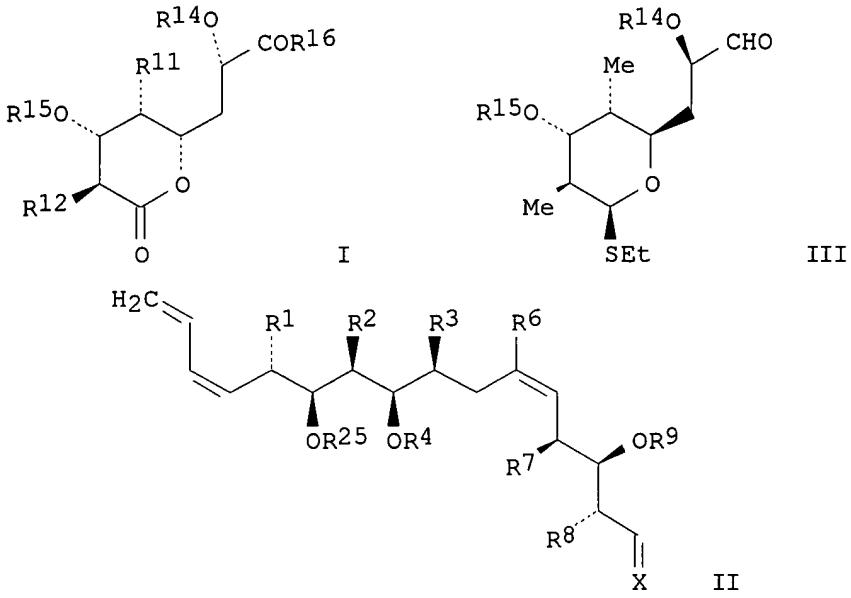
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6242616	B1	20010605	US 1999-455649	19991207
US 5789605	A	19980804	US 1996-759817	19961203
US 6031133	A	20000229	US 1998-21878	19980211
US 6096904	A	20000801	US 1998-121551	19980723
WO 2001042179	A1	20010614	WO 2000-US32996	20001206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002103387	A1	20020801	US 2000-730929	20001206
EP 1248761	A1	20021016	EP 2000-983924	20001206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:
US 1996-759817 A1 19961203
US 1998-21878 A1 19980211
US 1998-121551 A2 19980723
US 1999-455649 A 19991207
WO 2000-US32996 W 20001206

OTHER SOURCE(S): MARPAT 135:19496

GI



I III II

AB Prepn. of intermediates, such as I [R11, R12 = alkyl; R14, R15 = acid labile protecting groups; R16 = H, alkyl] and II [R1, R2, R7, R8 = alkyl; R3, R6, R16 = H, alkyl; R4, R9 = acid labile hydroxyl protecting group; R25 = oxidatively labile hydroxyl protecting group; X = :C(J)R16, a Wittig olefination formed from a pyranylalkyl ketone, such as I and II (X = P+Ph3I-)], for the synthesis of discodermolides and their analogs, which are useful as pharmaceuticals, was presented. Thus, synthon III (R14 = R15 = SiMe2CMe3) was prepd. via a multistep synthetic sequence starting from (2R)-3-hydroxy-2-methylpropanoic acid Me ester. The synthetic utility of II was subsequently demonstrated by its use in the prepn. of (-)-discodermolide.

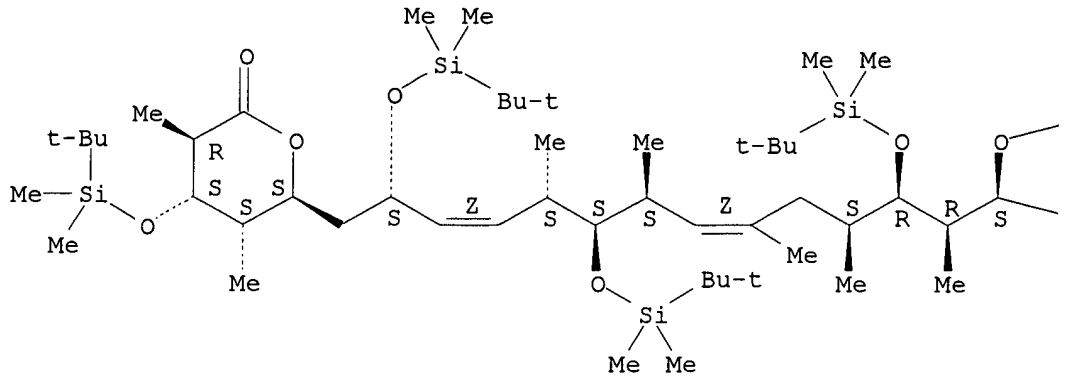
IT **252342-55-5 256921-06-9 256921-63-8 256921-65-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone derivs. for pharmaceutical use)

RN 252342-55-5 CAPLUS

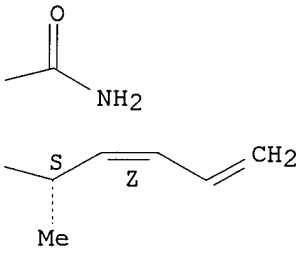
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



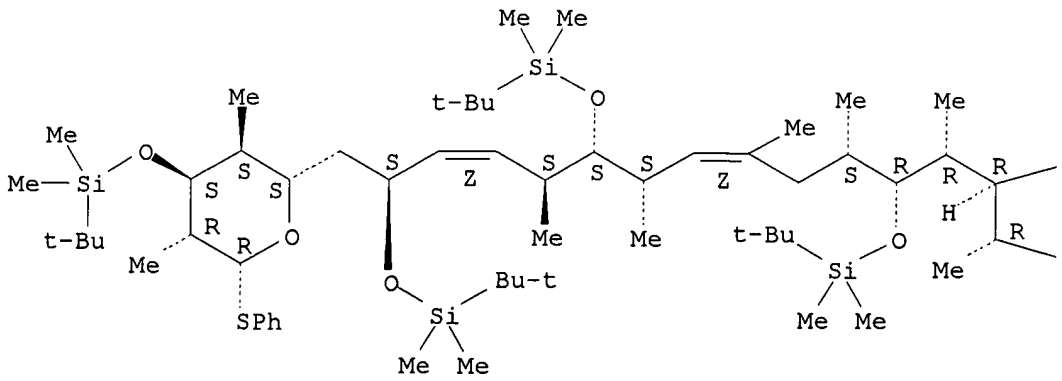
PAGE 1-B



RN 256921-06-9 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

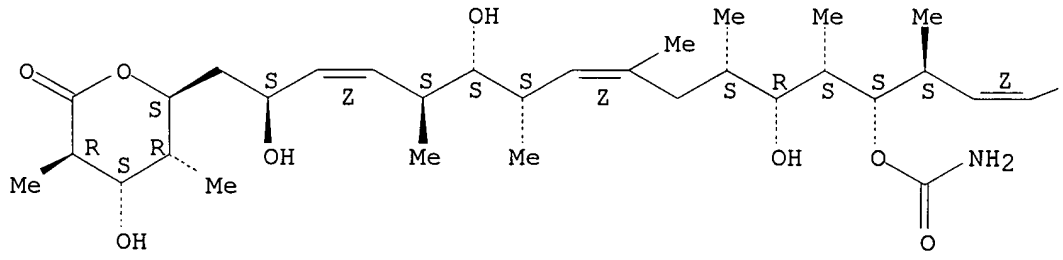
PAGE 1-A



L4 ANSWER 41 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:104725 CAPLUS
DOCUMENT NUMBER: 134:266105
TITLE: The chemistry and biology of discodermolide
AUTHOR(S): Kalesse, Markus
CORPORATE SOURCE: Inst. Org. Chem., Univ. Hannover, Hannover, 30167, Germany
SOURCE: ChemBioChem (2000), 1(3), 171-175
Published in: Angew. Chem., Int. Ed., 39(19)
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 16 refs. on the synthesis of discodermolide.
IT **127943-53-7P**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(chem. and biol. of discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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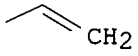


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:86649 CAPLUS
DOCUMENT NUMBER: 134:266136
TITLE: Solution Structure of (+)-Discodermolide
AUTHOR(S): Smith, Amos B., III; LaMarche, Matthew J.; Falcone-Hindley, Margaret
CORPORATE SOURCE: Department of Chemistry Monell Chemical Senses Center and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA,

19104, USA
SOURCE: Organic Letters (2001), 3(5), 695-698
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The soln. structure of (+)-discodermolide (I) has been detd. via 1- and 2-D NMR techniques in conjunction with Monte Carlo conformational anal. Taken together, the results demonstrate that in soln. I occupies a helical conformation remarkably similar to the solid state conformation.

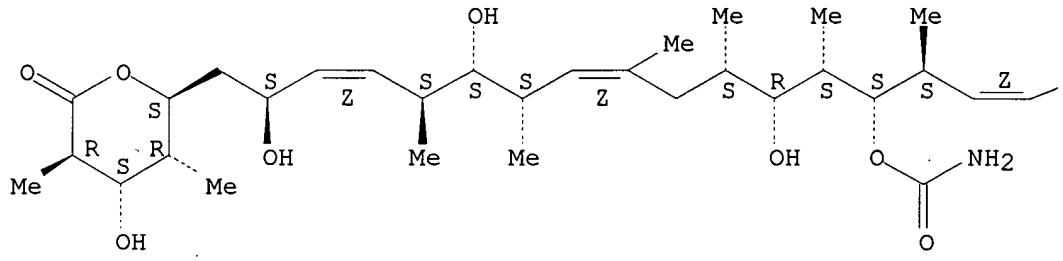
IT **127943-53-7**, (+)-Discodermolide
RL: PRP (Properties)
(conformational anal. of discodermolide by a combination of NMR techniques and computational methods)

RN 127943-53-7 CAPLUS

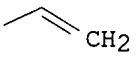
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:10271 CAPLUS
DOCUMENT NUMBER: 134:193282

TITLE: Acetylated Analogues of the Microtubule-Stabilizing Agent Discodermolide: Preparation and Biological Activity

AUTHOR(S): Gunasekera, Sarath P.; Longley, Ross E.; Isbrucker, Richard A.
CORPORATE SOURCE: Division of Biomedical Marine Research, Harbor Branch Oceanographic Institution, Fort Pierce, FL, 34946, USA

SOURCE: Journal of Natural Products (2001), 64(2), 171-174
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of eight discodermolide acetates have been prepd. using natural (+)-discodermolide and evaluated for in vitro cytotoxicity against the cultured murine P-388 leukemia cells. The acetylated analogs showed a significant variation of cytotoxicity and suggested the importance of C-11 and C-17 hydroxyl groups for potency. The prepn. and structure elucidation of the new analogs are described.

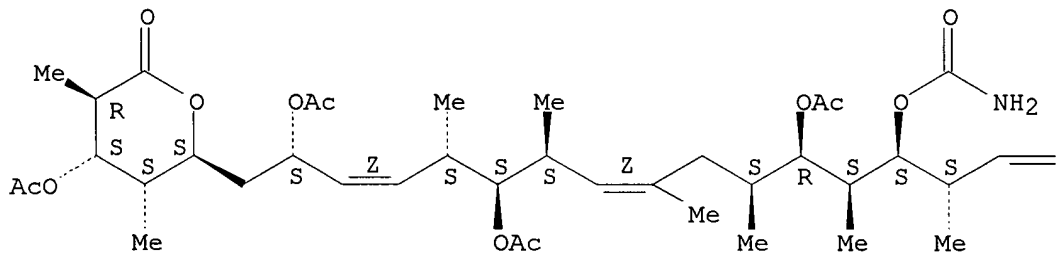
IT **299173-77-6P 299173-78-7P 299173-79-8P**
299173-80-1P 299173-81-2P 299173-82-3P
299173-83-4P 299173-84-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and anticancer activity of acetylated analogs of microtubule-stabilizing agent discodermolide)

RN 299173-77-6 CAPLUS

CN 2H-Pyran-2-one, 4-(acetyloxy)tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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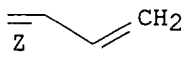
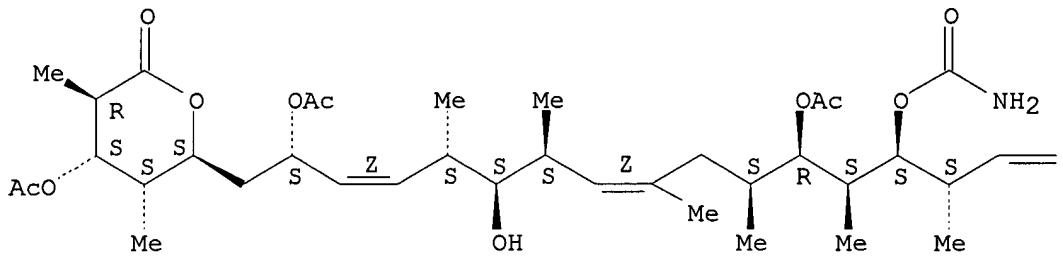


RN 299173-78-7 CAPLUS

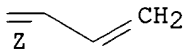
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,12-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-6-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



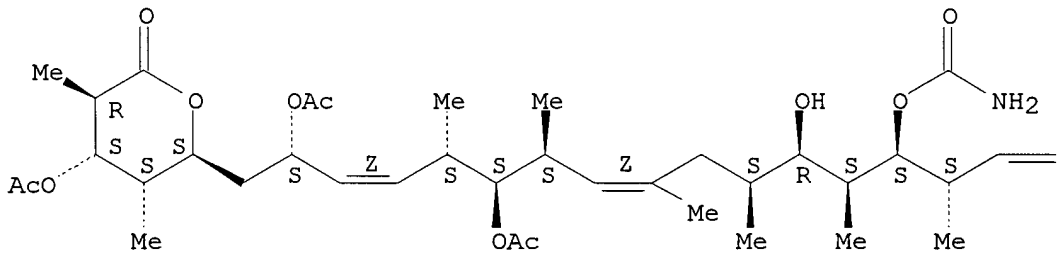
PAGE 1-B



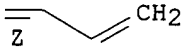
RN 299173-79-8 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



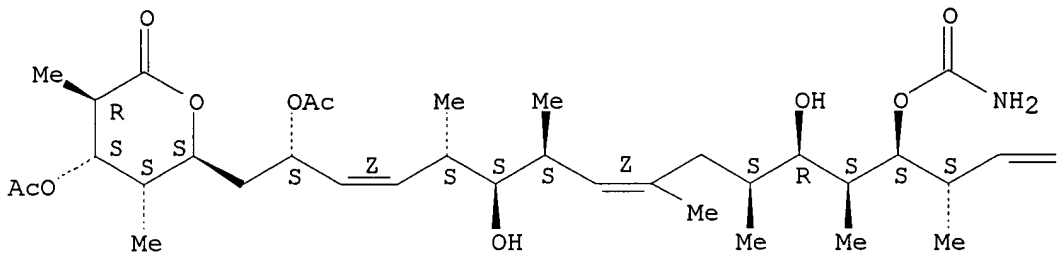
PAGE 1-B



RN 299173-80-1 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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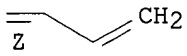
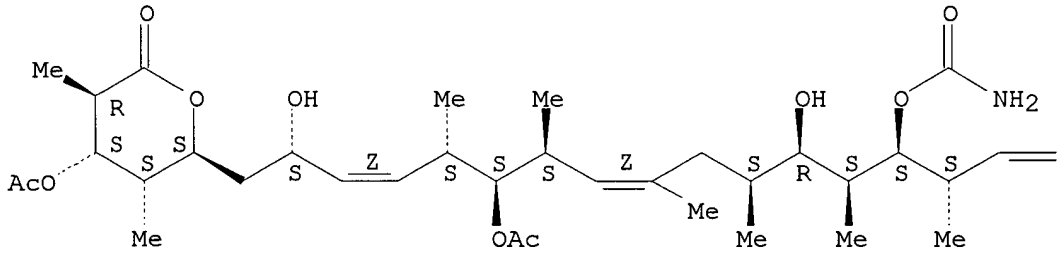


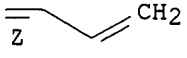
RN 299173-81-2 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-6-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

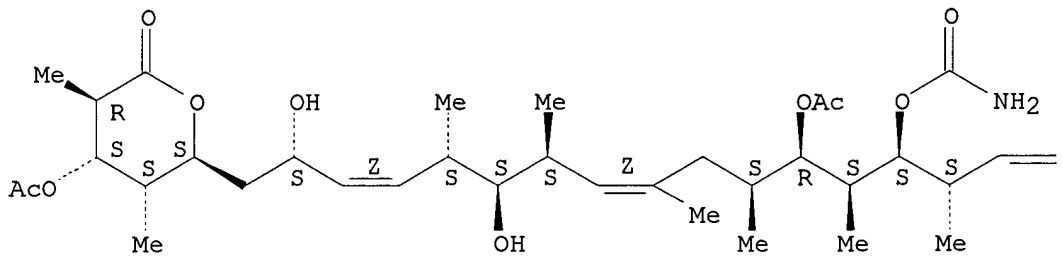


RN 299173-82-3 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16

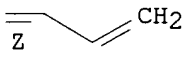
Z)-12-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,6-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



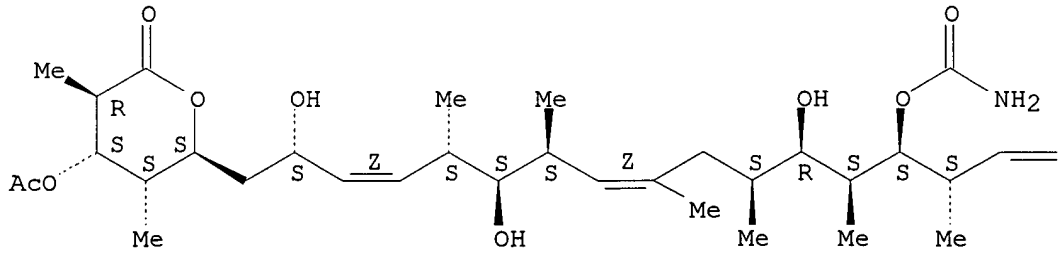
PAGE 1-B



RN 299173-83-4 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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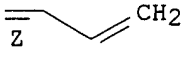
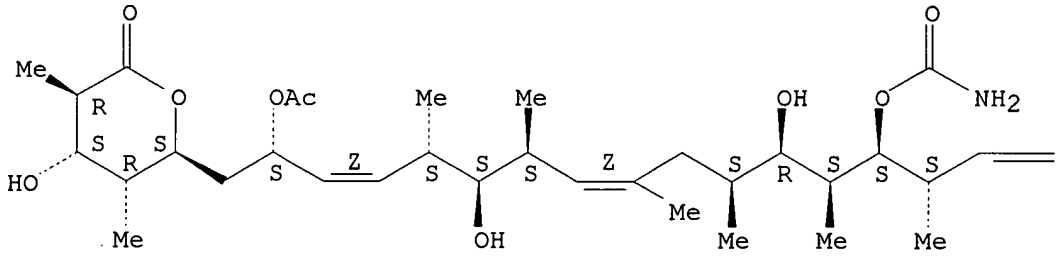


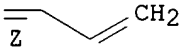
RN 299173-84-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



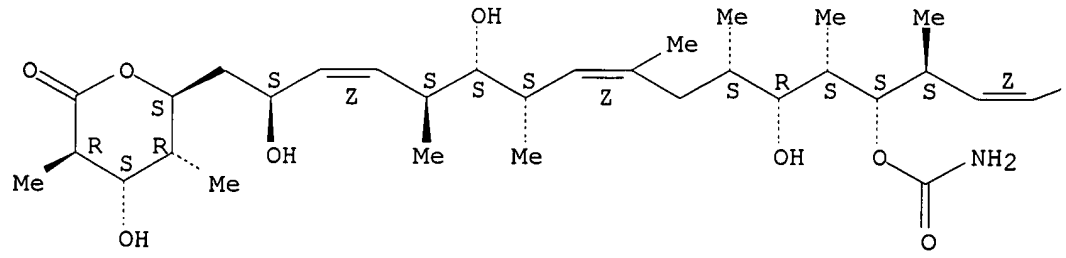
PAGE 1-B

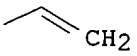


IT **127943-53-7**, (+)-Discodermolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and anticancer activity of acetylated analogs of microtubule-stabilizing agent discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:900785 CAPLUS
DOCUMENT NUMBER: 134:52230
TITLE: DNA manipulation methods and applications for construction of DNA assemblies expressing synthetic enzymes
INVENTOR(S): Ranganathan, Anand
PATENT ASSIGNEE(S): Qxyz Limited, UK
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077181	A2	20001221	WO 2000-GB2286	20000612
WO 2000077181	A3	20010510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1190045	A2	20020327	EP 2000-940533	20000612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1999-13694 A 19990611
WO 2000-GB2286 W 20000612

AB The invention comprises a method of assembling several DNA units in sequence in a DNA construct and all derivs. of this method. In particular the prodn. of synthetic enzymes is contemplated. Each DNA unit is provided with the same restriction enzyme recognition site at its 5' and 3' ends. The restriction recognition site at its 3' end being combined with a recognition site for a DNA modification enzyme. A DNA construct having the same or a compatible accessible restriction site, as provided in the DNA unit, is cleaved at the restriction site by the appropriate restriction enzyme. The desired DNA unit is then inserted into the DNA construct, this ligated product subsequently being brought into contact with a DNA modification enzyme such that the restriction site at the 3' end of the inserted DNA unit is abolished. The ligated product is then cleaved at the remaining unmodified restriction recognition site and a subsequent DNA unit is inserted. This process is repeated introducing each desired DNA unit to give a DNA construct contg. all the desired units in sequence. Using this methodol., the polyketide synthetase DEBS1-TE

(6-deoxyerythronolide B synthase thioesterase), a multienzyme that has the first of the three bimodular erythromycin DEBS enzymes fused with the erythromycin esterase, was constructed in a de novo fashion and shown to catalyze the synthesis of (2R,3S,4S,5R)-2,4-dimethyl-3,5-dihydroxy-n-hexanoid .delta.-lactone. A strategy employing the invention is also used to construct polyketide synthase domains/modules responsible for the biosynthesis of discodermolide (a highly potent anti-breast cancer drug), decarestrictin J (an anticholesterol compds.), and octalacin A or B (antitumor compds.).

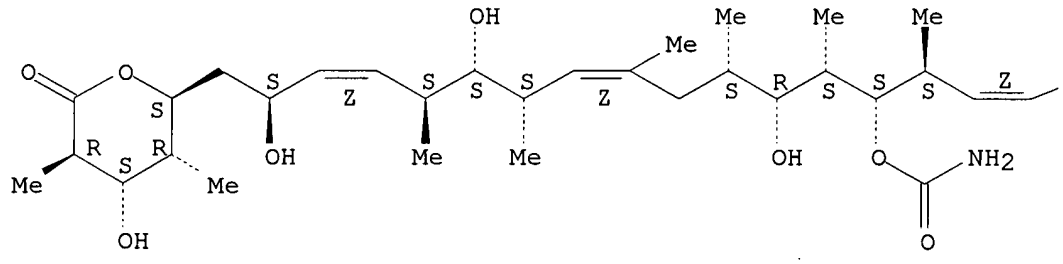
IT **127943-53-7P**, Discodermolide
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation)
(DNA manipulation methods and applications for construction of DNA assemblies expressing synthetic enzymes)

RN 127943-53-7 CAPLUS

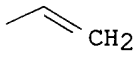
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 45 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:842651 CAPLUS
DOCUMENT NUMBER: 134:163177
TITLE: Natural products with Taxol-like anti-tumour activity
AUTHOR(S): Ceccarelli, Simona; Bell, Andrew A.; Gennari, Cesare
CORPORATE SOURCE: Dipartimento di Chimica Organica e Industriale, Centro CNR (Sost. Org. Nat.), Universita degli Studi di Milano, Milan, 20133, Italy
SOURCE: Seminars in Organic Synthesis, Summer School "A. Corbella", 25th, Gargnano, Italy, June 12-16, 2000 (2000), 91-115. Societa Chimica Italiana: Rome, Italy.
CODEN: 69AQRY
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 53 refs. on natural products with taxol-like antitumor activity, including sarcodictyins A and B, eleutherobin, epothilones A and B, discodermolide, laulimalide and isolaulimalide. These natural products exert their cytotoxic effect by destabilization of the microtubule structure and promotion of disassembly of microtubules into tubulin.

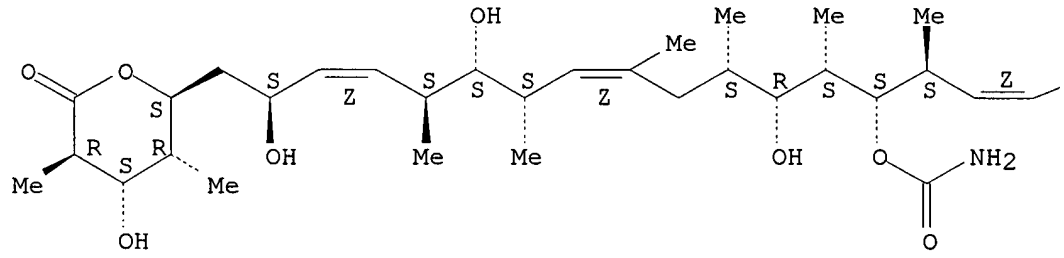
IT **127943-53-7P**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(natural products with taxol-like antitumor activity)

RN 127943-53-7 CAPLUS

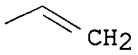
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 46 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2000:842309 CAPLUS
DOCUMENT NUMBER:	134:25333
TITLE:	Primers for the detection of tubulin mutations leading to paclitaxel resistance in human tumor cells
INVENTOR(S):	Cabral, Fernando
PATENT ASSIGNEE(S):	Board of Regents of the University of Texas System, USA
SOURCE:	PCT Int. Appl., 106 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000071752 A2 20001130 WO 2000-US13610 20000518
WO 2000071752 A3 20010301
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1179094 A2 20020213 EP 2000-936034 20000518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-135047P P 19990520
WO 2000-US13610 W 20000518

AB Tubulin mutations commonly assocd. with resistance to paclitaxel are defined, and PCR allele-specific primers capable of detecting the mutations in DNA from tumor cells are described as well as method for treating paclitaxel-resistant cells in tumors. A simple, rapid, and cost effective means for detecting paclitaxel-resistant cells in tumor biopsies from patients receiving paclitaxel therapy is disclosed. The characterization of a no. of paclitaxel-resistant mutants of CHO cells is described. Paclitaxel resistance is assocd. with lower ds.p. of microtubules and dependence is assocd. with very low levels of polymn. Mutations were clustered in a 14 amino acid peptide (214-threonine-228-leucine) and many of the mutations affecting leucine residues in the peptide. Further, many of the substitutions required at least two nucleotide changes.

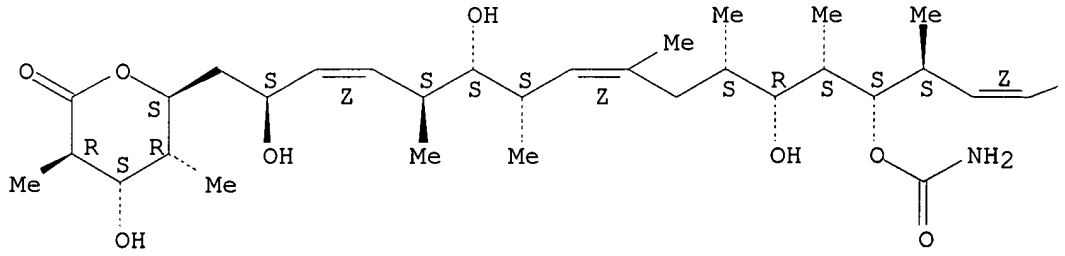
IT **127943-53-7D**, Discodermolide, analogs
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(resistance to; primers for detection of tubulin mutations leading to paclitaxel resistance in human tumor cells)

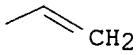
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





L4 ANSWER 47 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:842015 CAPLUS
DOCUMENT NUMBER: 134:21458
TITLE: Tocopherols as an emulsion vehicle for poorly soluble drugs
INVENTOR(S): Lambert, Karel J.; Constantinides, Panayiotis P.; Quay, Steven C.; Tustian, Alexander K.
PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071163	A1	20001130	WO 2000-US13572	20000517
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1185301	A1	20020313	EP 2000-937583	20000517
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010794	A	20020604	BR 2000-10794	20000517

PRIORITY APPLN. INFO.:
US 1999-317495 A 19990524
US 1999-317499 A 19990524
US 1999-156128P P 19990927
WO 2000-US13572 W 20000517

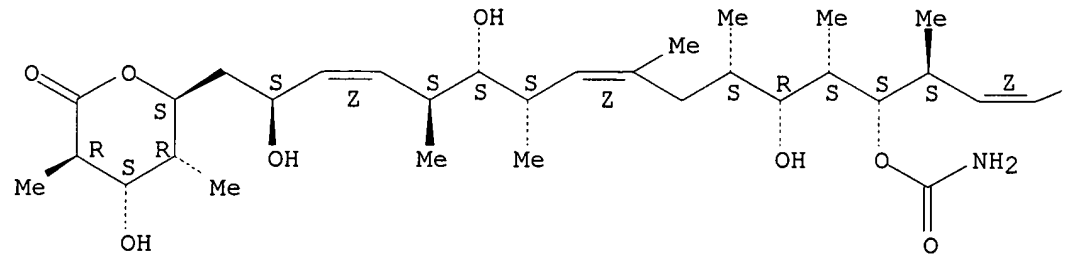
AB The present invention discloses an emulsion of incorporating one or more tocols, a co-solvent and stabilized by biocompatible surfactants, as a vehicle or carrier for poorly sol. therapeutic drugs, which is substantially ethanol free and which can be administered to animals or humans by various routes. Also included in the emulsion is PEGylated vitamin E (TPGS), which includes polyethylene glycol subunits attached by a succinic acid diester at the ring hydroxyl of vitamin E and serves as a primary surfactant, stabilizer and a secondary solvent in tocol emulsions.. An i.v. emulsion contained paclitaxel 1, .alpha.-tocopherol 3, TPGS 2, ascorbyl-6-palmitate 0.25, sorbitol 5 %, triethanolamine q.s. to pH 6.8, and water q.s. to 100 mL.

IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tocopherols as emulsion vehicles for poorly sol. drugs)

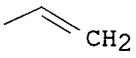
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 48 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:699192 CAPLUS
DOCUMENT NUMBER: 133:281651
TITLE: synthesis, antitumor activity and formulations of discodermolide acetates
INVENTOR(S): Gunasekera, Sarath P.; Longley, Ross E.
PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution, Inc., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127406	A	20001003	US 1999-412552	19991005

PRIORITY APPLN. INFO.: US 1998-103806P P 19981009
OTHER SOURCE(S): MARPAT 133:281651

AB Novel acetate analogs of compds. from the marine sponge Discodermia dissoluta have been prepd. These compds. have been shown to have activity against mammalian cancer cells, and can be used in treating human patients which host cancer cells, including leukemia, melanoma, breast, colon, CNS, renal, ovarian, prostate, and lung tumors. Formulations are given.

IT **299173-77-6P 299173-78-7P 299173-79-8P**
299173-80-1P 299173-81-2P 299173-82-3P
299173-83-4P 299173-84-5P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

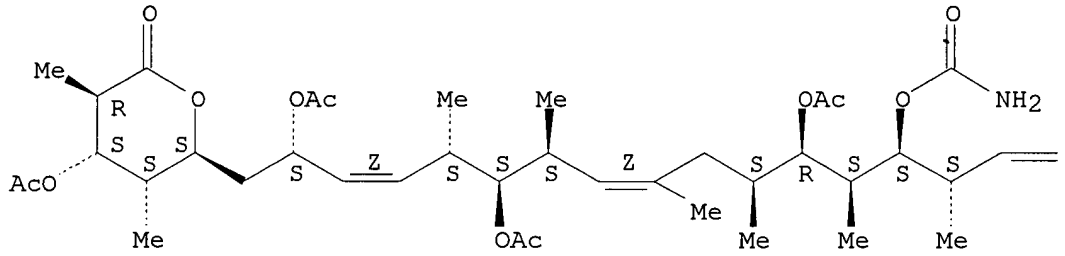
effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, antitumor activity and formulations of discodermolide acetates)

RN 299173-77-6 CAPLUS

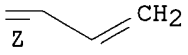
CN 2H-Pyran-2-one, 4-(acetyloxy)tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

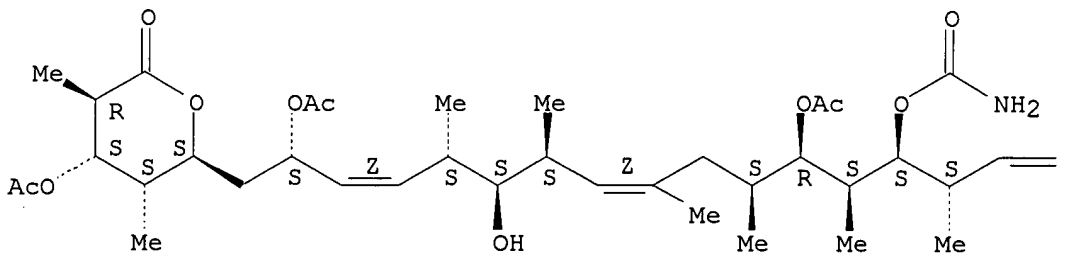


RN 299173-78-7 CAPLUS

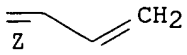
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,12-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-6-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



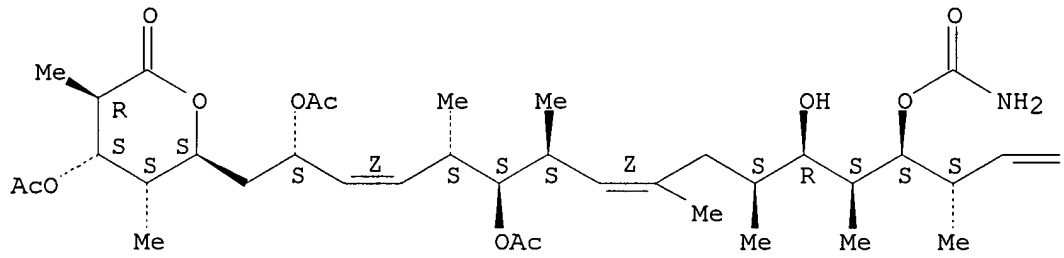
PAGE 1-B



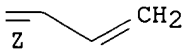
RN 299173-79-8 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2,6-bis(acetyloxy)-14-[(aminocarbonyl)oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



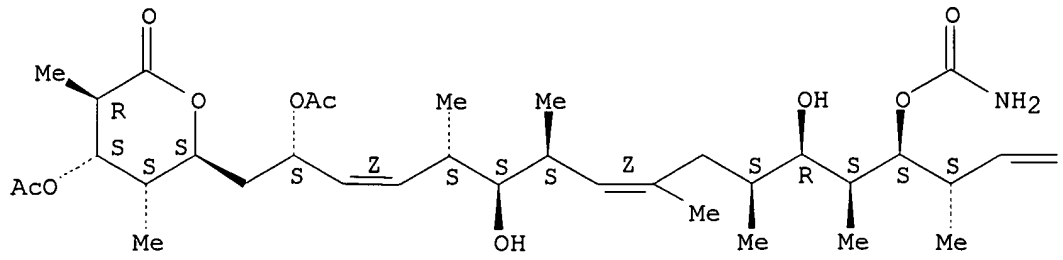
PAGE 1-B



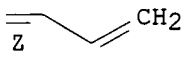
RN 299173-80-1 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



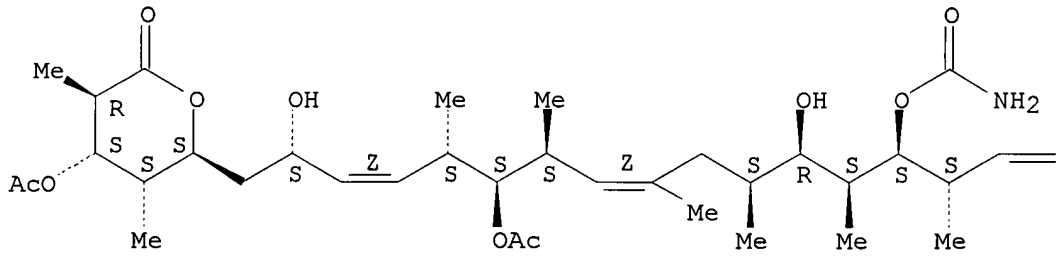
PAGE 1-B



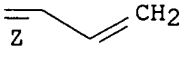
RN 299173-81-2 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-6-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



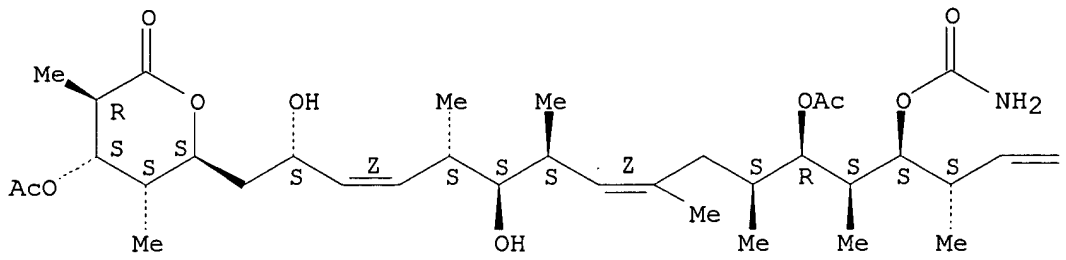
PAGE 1-B



RN 299173-82-3 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-12-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,6-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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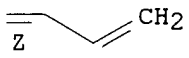
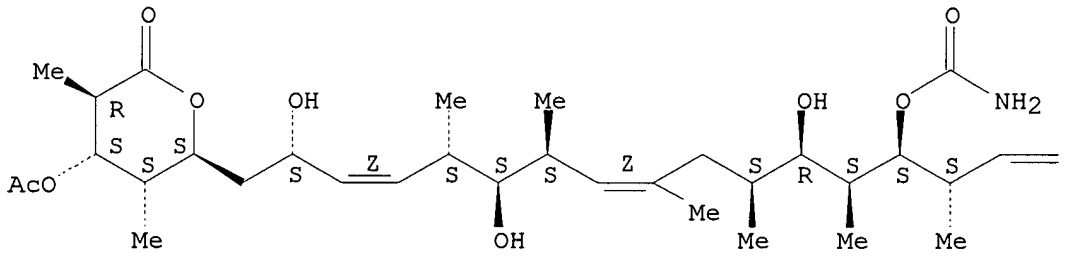


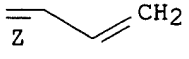
RN 299173-83-4 CAPLUS
CN 2H-Pyran-2-one, 4-(acetyloxy)-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

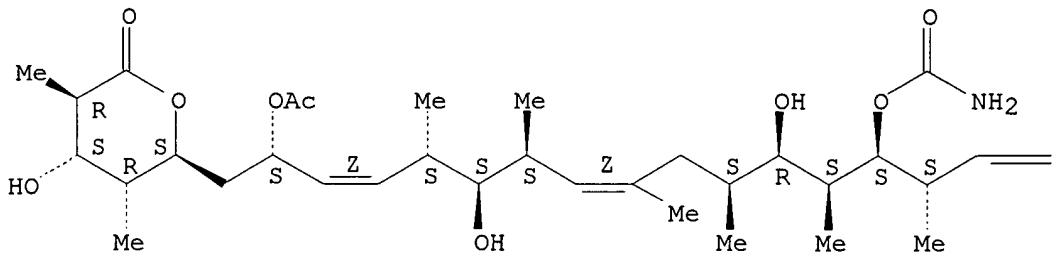


RN 299173-84-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-2-

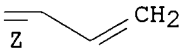
(acetyloxy)-14-[(aminocarbonyl)oxy]-6,12-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



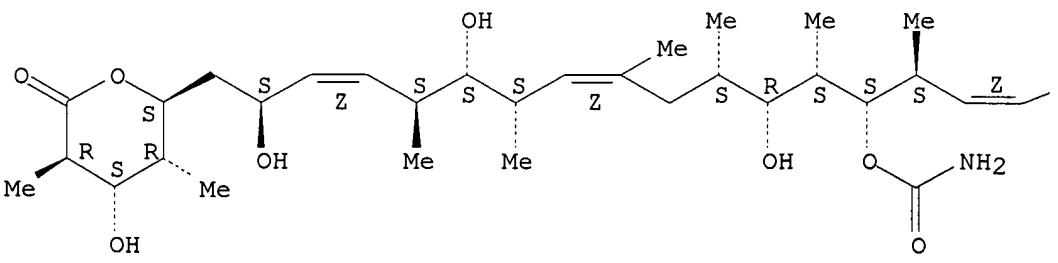
IT **127943-53-7**, Discodermolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, antitumor activity and formulations of discodermolide acetates)

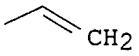
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

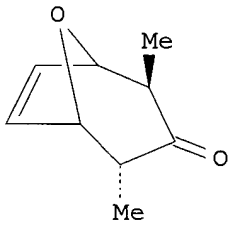
PAGE 1-A





REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 49 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:690122 CAPLUS
DOCUMENT NUMBER: 134:4808
TITLE: High stereochemical diversity and applications for the synthesis of marine natural products: a library of carbohydrate mimics and polyketide segments
AUTHOR(S): Misske, Andrea M.; Hoffmann, H. Martin R.
CORPORATE SOURCE: Department of Organic Chemistry, University of Hannover, Hannover, 30167, Germany
SOURCE: Chemistry--A European Journal (2000), 6(18), 3313-3320
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:4808
GI



I

AB A powerful concept for the rapid assembly of a series of twenty-four homochiral building blocks from simple racemic trans-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one (I) was described. The series comprises eight stereochem. pentades of anomeric [3.3.1]lactone acetals, eight stereochem. tetrades of anomeric carbohydrate mimics, and eight stereotetrades of acyclic polypropionate units. The utility of these enantiopure materials (av. 94% ee) in natural product synthesis is demonstrated and shown to complement the popular aldol method.

IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(prepn. of a library of carbohydrate mimics and polyketide segments with stereochem. diversity and applications for the synthesis of marine natural products)

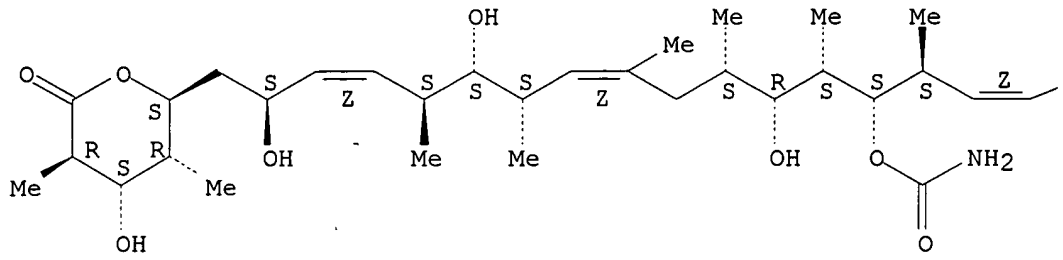
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

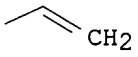
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A

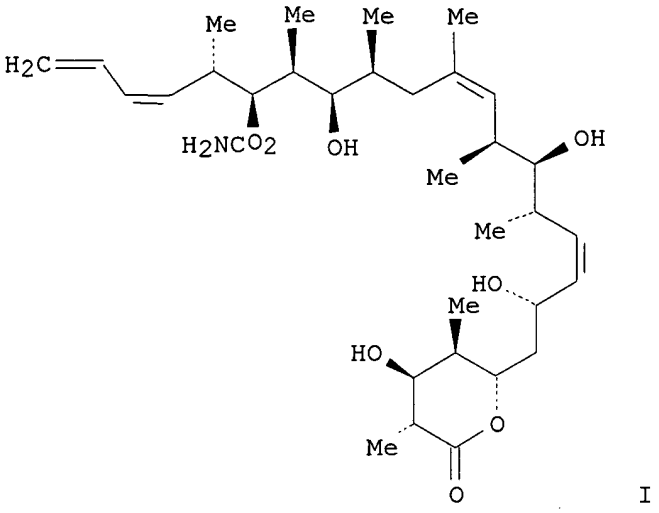


PAGE 1-B



REFERENCE COUNT: 177 THERE ARE 177 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 50 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:597937 CAPLUS
DOCUMENT NUMBER: 133:335118
TITLE: Evolution of a Gram-Scale Synthesis of (+)-Discodermolide
AUTHOR(S): Smith, Amos B., III; Beauchamp, Thomas J.; LaMarche, Matthew J.; Kaufman, Michael D.; Qiu, Yuping; Arimoto, Hirokazu; Jones, David R.; Kobayashi, Kaoru
CORPORATE SOURCE: Department of Chemistry Monell Chemical Senses Center and Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of the American Chemical Society (2000), 122(36), 8654-8664
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:335118
GI



I

AB An efficient, highly convergent, stereocontrolled total synthesis of the potent antimitotic agent (+)-discodermolide (I) has been achieved on gram scale. Key elements of the successful strategy include (1) elaboration of three advanced fragments from a common precursor (CP) which embodies the repeating stereochem. triad of the discodermolide backbone, (2) .sigma.-bond installation of the Z trisubstituted olefin, exploiting a modified Negishi cross-coupling reaction, (3) synthesis of a late-stage phosphonium salt utilizing high pressure, and (4) Wittig installation of the Z disubstituted olefin and the terminal (Z)-diene.

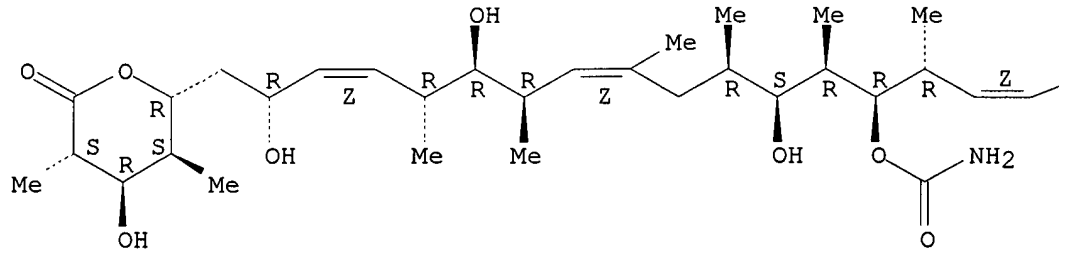
IT **154335-30-5P**, (-)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(evolution of a gram-scale synthesis of (+)-discodermolide)

RN 154335-30-5 CAPLUS

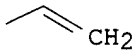
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

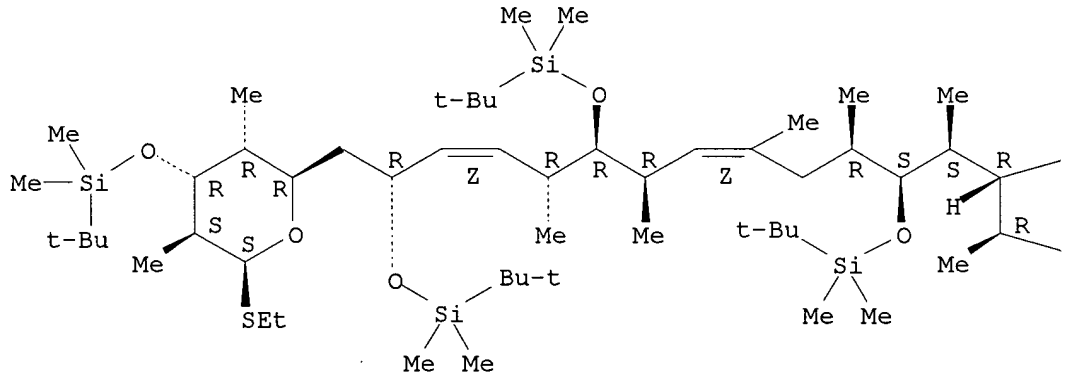


IT **208984-62-7P 208984-63-8P 252342-47-5P**
252342-48-6P 252342-55-5P 303728-14-5P
303728-15-6P 303728-16-7P 303728-17-8P
303728-25-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(evolution of a gram-scale synthesis of (+)-discodermolide)

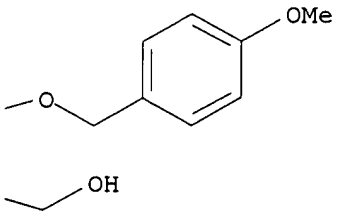
RN 208984-62-7 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4S,5S,6R,8Z,10R,11R,12R,13Z,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

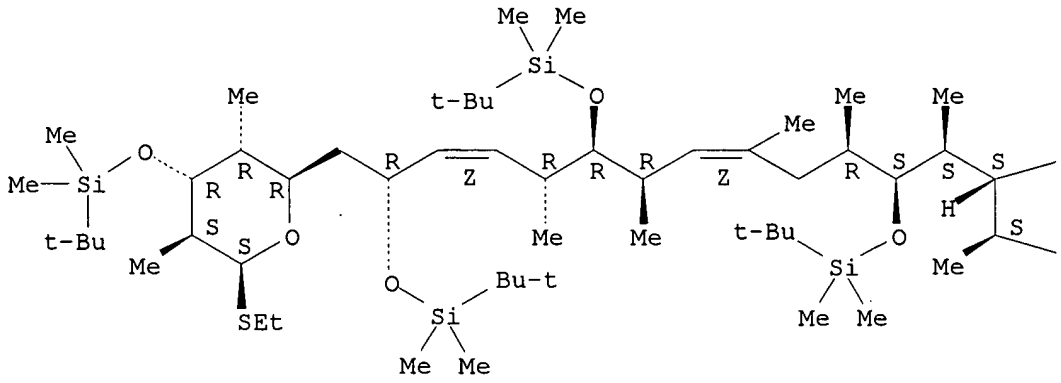


RN 208984-63-8 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-

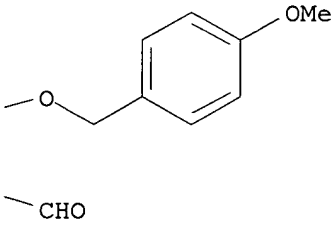
16-[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4S,5S,6R,8Z,10R,11R,12R,13Z,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



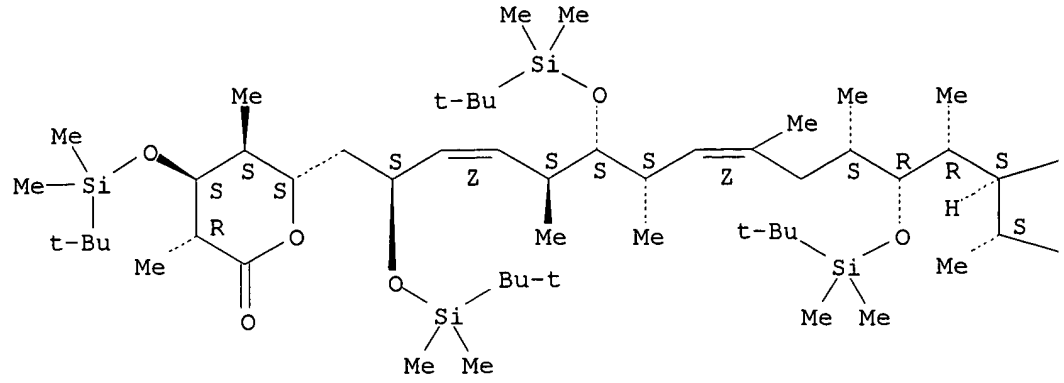
PAGE 1-B



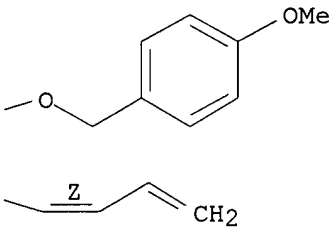
RN 252342-47-5 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



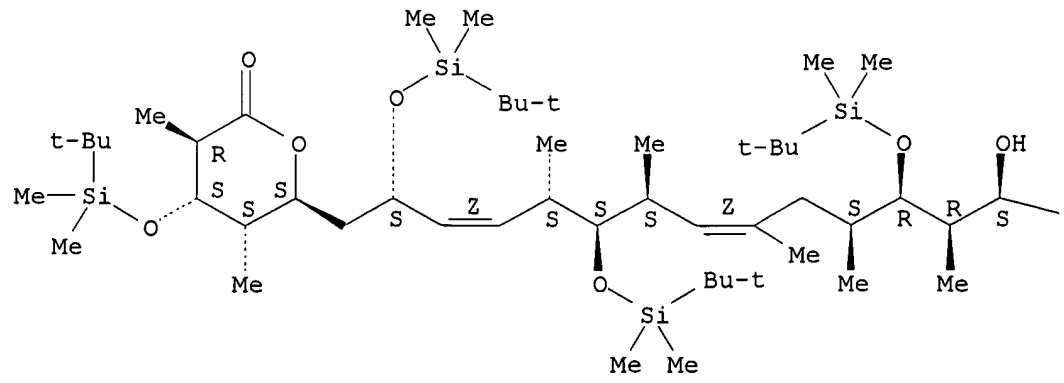
PAGE 1-B



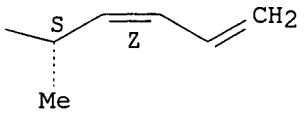
RN 252342-48-6 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



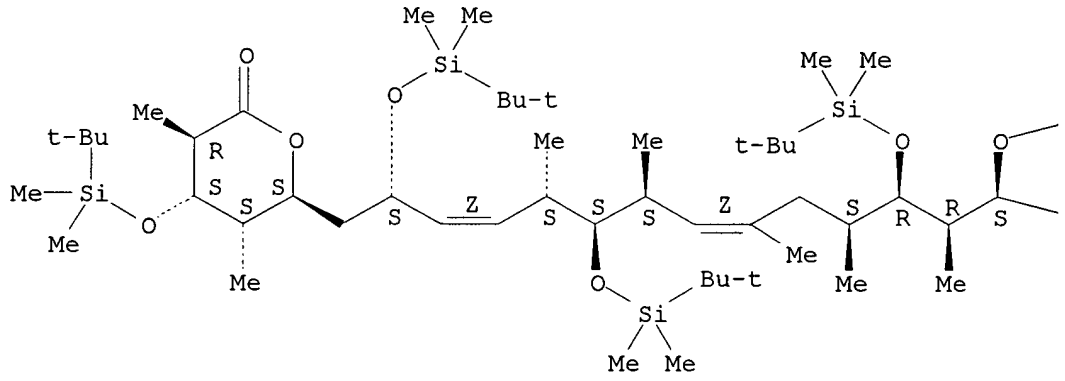
PAGE 1-B



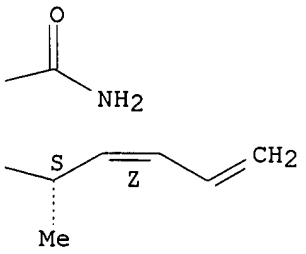
RN 252342-55-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

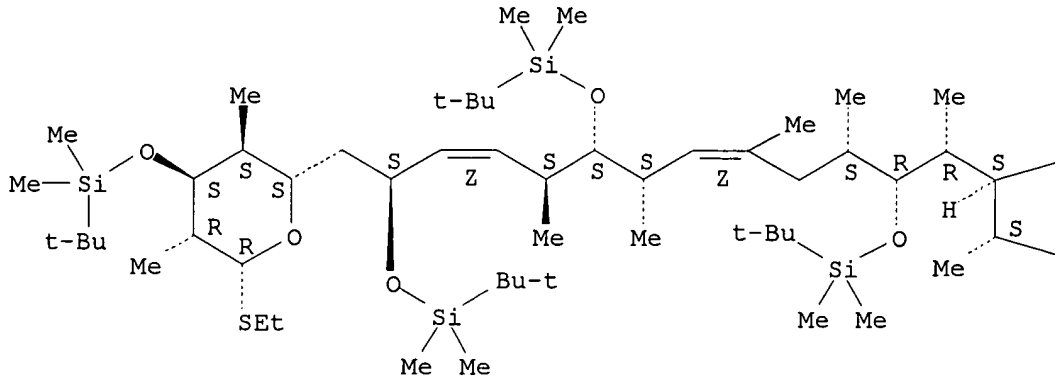


RN 303728-14-5 CAPLUS
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-

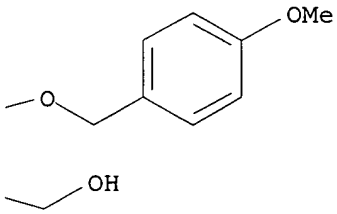
(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



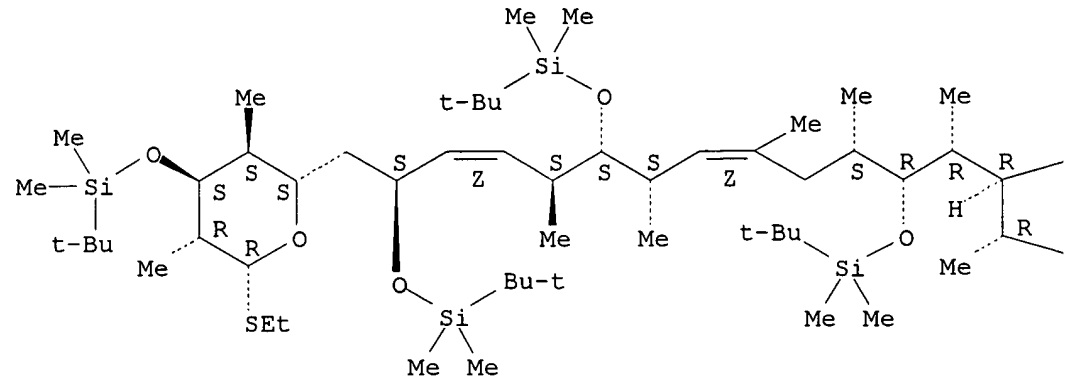
PAGE 1-B



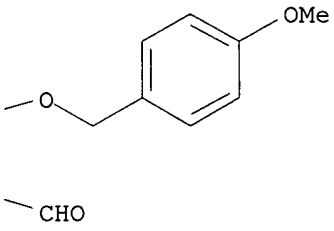
RN 303728-15-6 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4R,5R,6S,8Z,10S,11S,12S,13Z,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



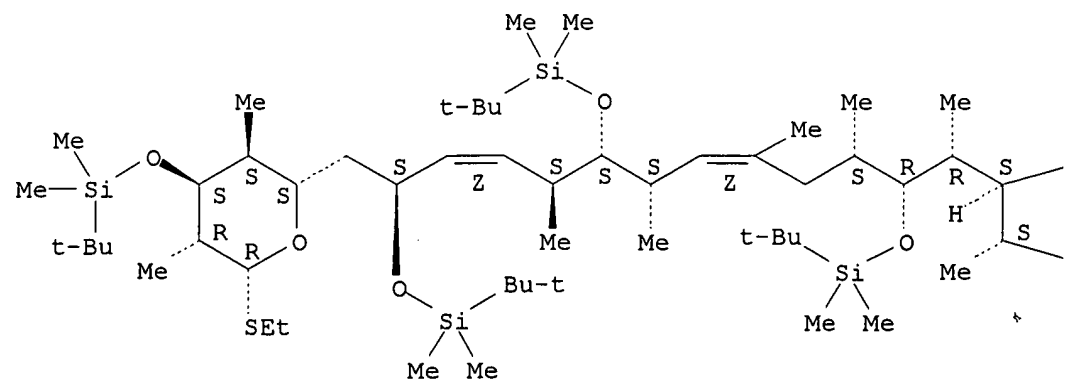
PAGE 1-B



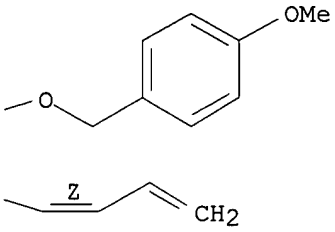
RN 303728-16-7 CAPLUS
CN 4,16-Dioxa-3,17-disilanonadeca-6,11-diene, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[(2S,3S,4S,5R,6R)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]methyl]-15-[(1R,2S,3S,4Z)-2-[(4-methoxyphenyl)methoxy]-1,3-dimethyl-4,6-heptadienyl]-2,2,3,3,8,10,12,14,17,17,18,18-dodecamethyl-, (5S,6Z,8S,9S,10S,11Z,14S,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



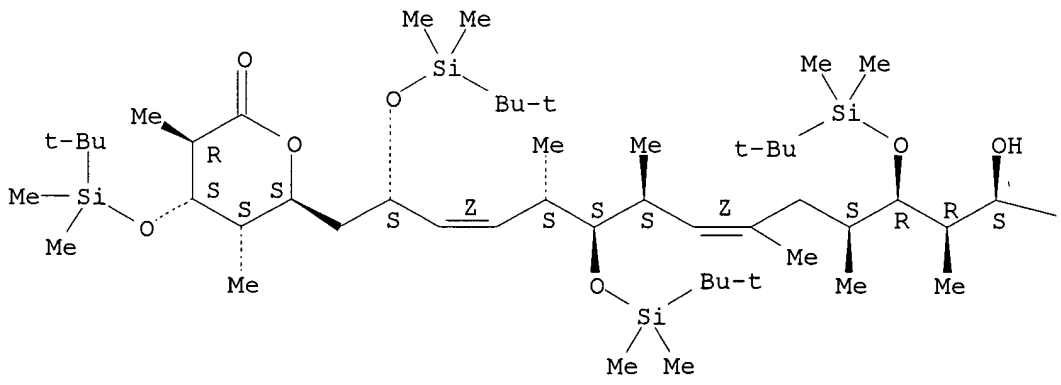
RN 303728-17-8 CAPLUS
CN 1,4-Cyclohexadiene-1,2-dicarbonitrile, 4,5-dichloro-3,6-dioxo-, compd. with (3R,4S,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-2H-pyran-2-one (1:1) (9CI) (CA INDEX NAME)

CM 1

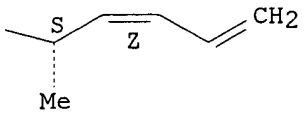
CRN 252342-48-6
CMF C56 H110 O7 Si4

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A

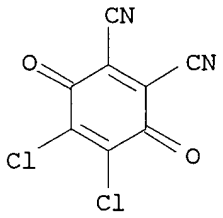


PAGE 1-B



CM 2

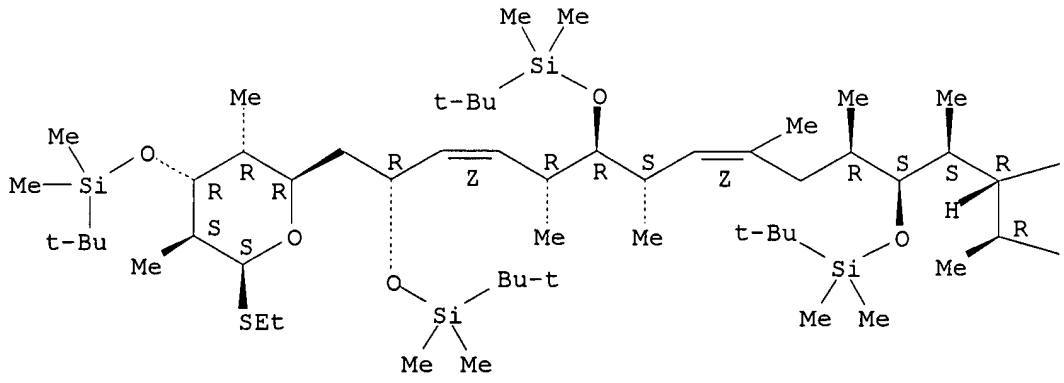
CRN 84-58-2
CMF C8 Cl2 N2 O2



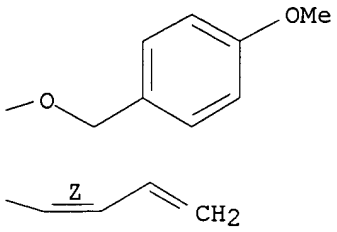
RN 303728-25-8 CAPLUS
CN 4,16-Dioxa-3,17-disilanonadeca-6,11-diene, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]methyl]-15-[(1S,2R,3R,4Z)-2-[(4-methoxyphenyl)methoxy]-1,3-dimethyl-4,6-heptadienyl]-2,2,3,3,8,10,12,14,17,17,18,18-dodecamethyl-, (5R,6Z,8R,9R,10S,11Z,14R,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



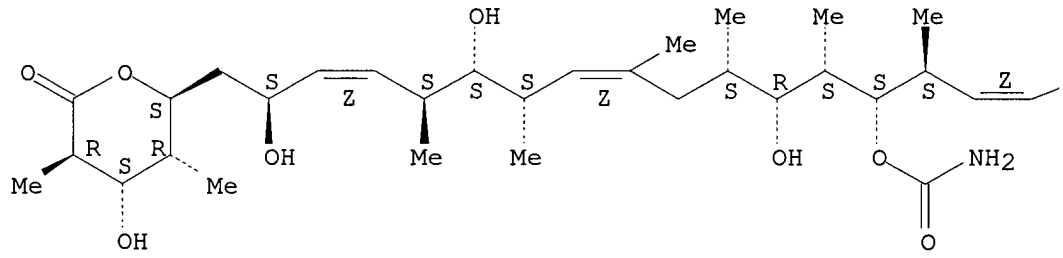
PAGE 1-B



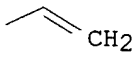
IT **127943-53-7P,** (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(evolution of a gram-scale synthesis of (+)-discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 101 THERE ARE 101 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 51 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:595470 CAPLUS
DOCUMENT NUMBER: 133:335117
TITLE: Synthesis of (+)-discodermolide and analogues by control of asymmetric induction in aldol reactions of .gamma.-chiral (Z)-enals
AUTHOR(S): Paterson, I.; Florence, G. J.
CORPORATE SOURCE: University Chemical Laboratory, Cambridge, CB2 1EW, UK
SOURCE: Tetrahedron Letters (2000), 41(35), 6935-6939

CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:335117

AB The boron-mediated aldol reactions of (Z)-enals proceed with high levels of 1,4-stereo induction arising from the .gamma.-substituent. Reagent control from (+)-Ipc2BCl can be used effectively to overturn this substrate bias, thus enabling the stereocontrolled formation of (+)-discodermolide and related analogs.

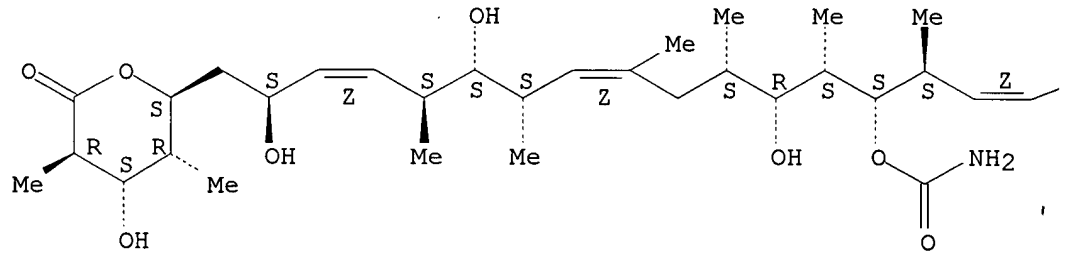
IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of (+)-discodermolide and analogs by control of asym. induction in aldol reactions of chiral enals)

RN 127943-53-7 CAPLUS

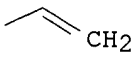
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

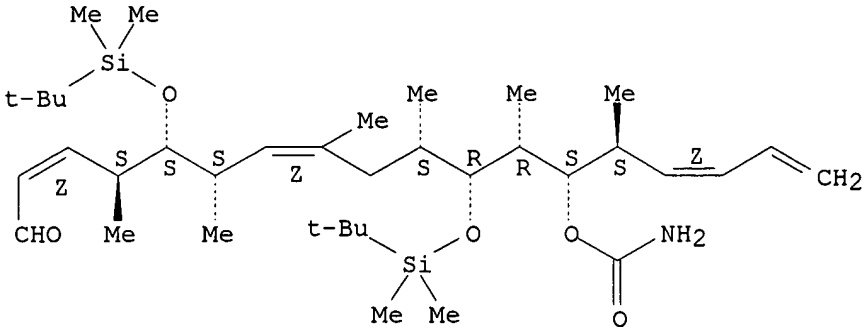


IT **261968-08-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of (+)-discodermolide and analogs by control of asym. induction in aldol reactions of chiral enals)

RN 261968-08-5 CAPLUS

CN 2,7,15,17-Octadecatetraenal, 13-[(aminocarbonyl)oxy]-5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



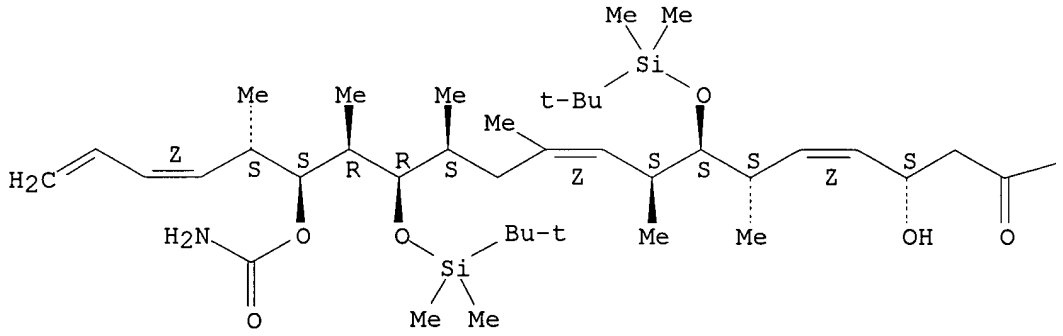
IT **261968-25-6P 303964-32-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of (+)-discodermolide and analogs by control of asym. induction in aldol reactions of chiral enals)

RN 261968-25-6 CAPLUS

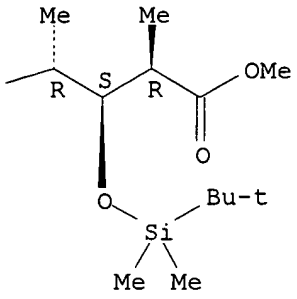
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-5-oxo-, methyl ester, (2R,3S,4R,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



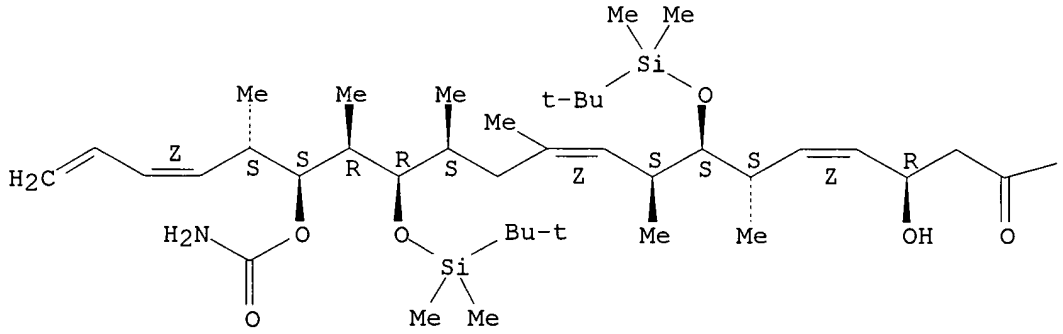
PAGE 1-B



RN 303964-32-1 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-5-oxo-, methyl ester, (2R,3S,4R,7R,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



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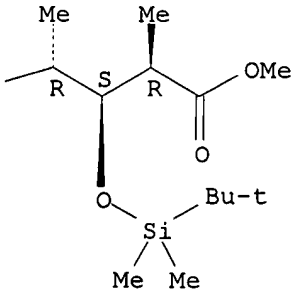
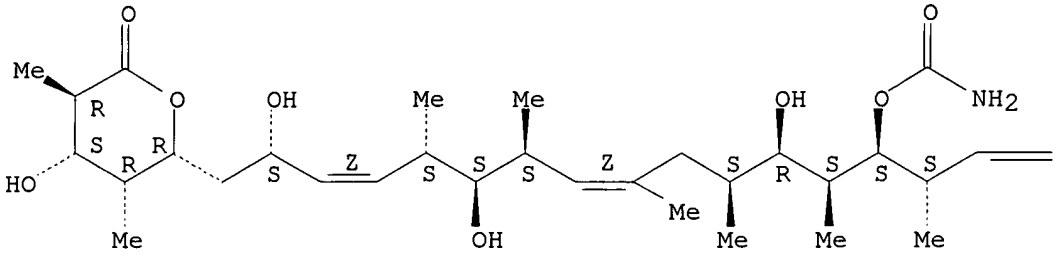


IT **303964-33-2P 303964-34-3P 303964-35-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of (+)-discodermolide and analogs by control of asym. induction in aldol reactions of chiral enals)

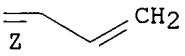
RN 303964-33-2 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



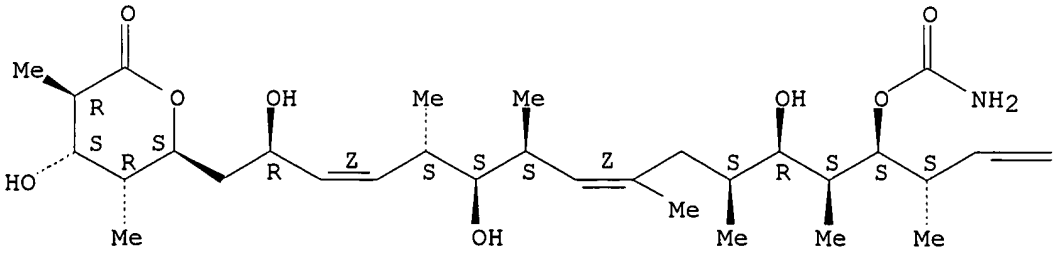
PAGE 1-B



RN 303964-34-3 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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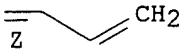
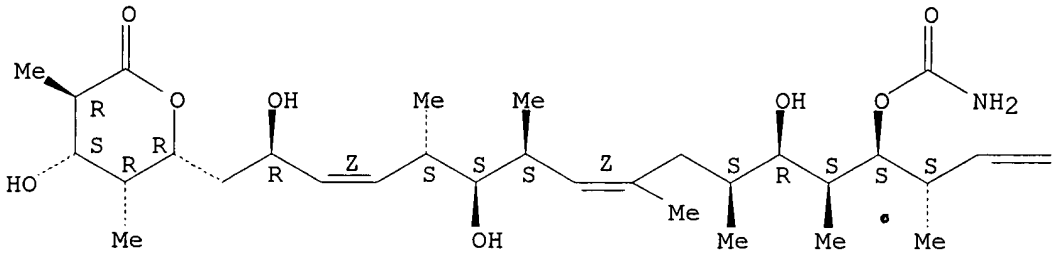


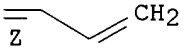
RN 303964-35-4 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:531688 CAPLUS
DOCUMENT NUMBER: 133:135166
TITLE: Preparation of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone derivatives for pharmaceutical use
INVENTOR(S): Smith, Amos B., III; Qiu, Yuping; Kaufman, Michael; Arimoto, Hirokazu; Jones, David R.; Kobayashi, Kaoru; Beauchamp, Thomas J.
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: U.S., 83 pp., Cont.-in-part of U.S. 5,789,605.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6

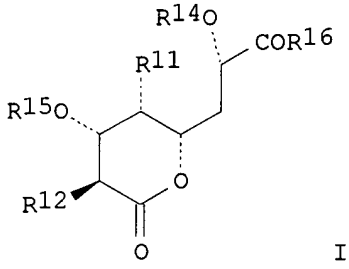
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6096904	A	20000801	US 1998-121551	19980723
US 5789605	A	19980804	US 1996-759817	19961203
WO 2000004865	A2	20000203	WO 1999-US16369	19990720
WO 2000004865	A3	20000921		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9952190	A1	20000214	AU 1999-52190	19990720
AU 749844	B2	20020704		
EP 1105383	A2	20010613	EP 1999-937330	19990720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002521317	T2	20020716	JP 2000-560858	19990720
US 6242616	B1	20010605	US 1999-455649	19991207

PRIORITY APPLN. INFO.:
US 1996-759817 A2 19961203
US 1998-21878 A1 19980211
US 1998-121551 A 19980723
WO 1999-US16369 W 19990720

OTHER SOURCE(S): MARPAT 133:135166

GI



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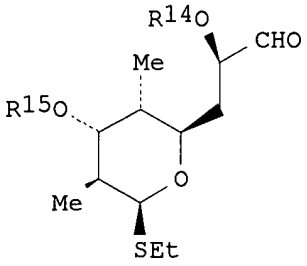


II

AB Prepn. of intermediates, such as I [R11, R12 = alkyl; R14, R15 = acid labile protecting groups; R16 = H, alkyl], for the synthesis of discodermolides and their analogs, which are useful as pharmaceuticals, was presented. Thus, synthon II (R14 = R15 = SiMe2CMe3) was prepd. via a multistep synthetic sequence starting from (2R)-3-hydroxy-2-methylpropanoic acid Me ester. The synthetic utility of II was subsequently demonstrated by its use in the prepn. of (-)-discodermolide.

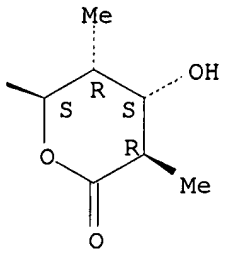
IT **252342-55-5 256921-06-9 256921-63-8 256921-65-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone derivs. for pharmaceutical use)

RN 252342-55-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

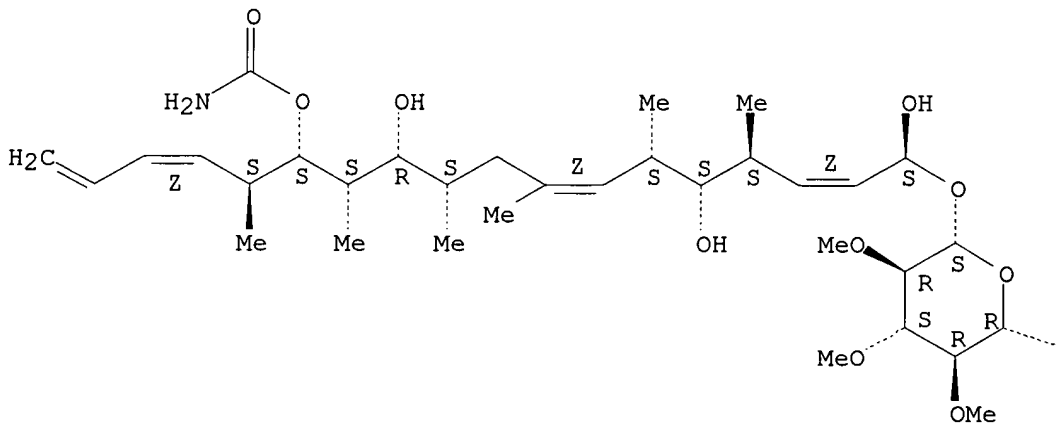
PAGE 1-B



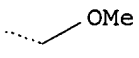
RN 256921-48-9 CAPLUS
CN .beta.-D-Glucopyranoside, (1S,2Z,4S,5S,6S,7Z,10S,11R,12S,13S,14S,15Z)-13-[(aminocarbonyl)oxy]-1,5,11-trihydroxy-4,6,8,10,12,14-hexamethyl-2,7,15,17-octadecatetraenyl 2,3,4,6-tetra-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 53 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:401136 CAPLUS
DOCUMENT NUMBER: 133:261225
TITLE: Taxol and discodermolide represent a synergistic drug combination in human carcinoma cell lines
AUTHOR(S): Martello, Laura A.; McDaid, Hayley M.; Regl, Donna Lee; Yang, Chia-Ping H.; Meng, Dongfang; Pettus, Thomas R. R.; Kaufman, Michael D.; Arimoto, Hirokazu; Danishefsky, Samuel J.; Smith, Amos B., III; Horwitz, Susan Band
CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: Clinical Cancer Research (2000), 6(5), 1978-1987
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

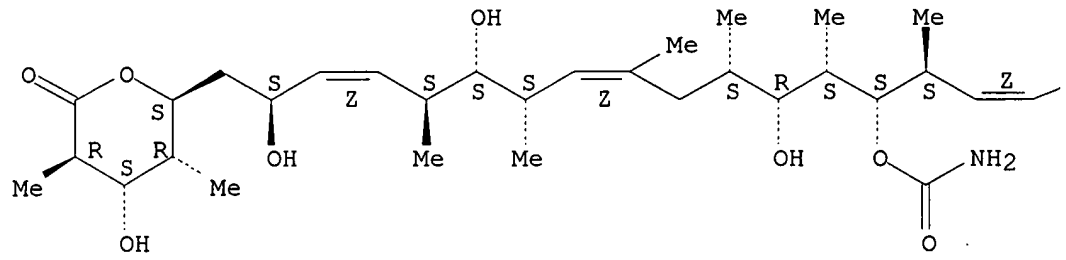
AB Recently, three natural products have been identified, the epothilones, eleutherobin, and discodermolide, whose mechanism of action is similar to that of Taxol in that they stabilize microtubules and block cells in the mitotic phase of the cell cycle. In this report, we have compared and contrasted the effects of these new agents in Taxol-sensitive and -resistant cell lines. We also have taken advantage of a human lung carcinoma cell line, A549-T12, that was isolated as a Taxol-resistant cell line and found to require low concns. of Taxol (2-6 nM) for normal cell division. This study then examd. the ability of these new compds. to substitute for Taxol in sustaining the growth of A549-T12 cells. Immunofluorescence and flow cytometry have both indicated that the epothilones and eleutherobin, but not discodermolide, can substitute for Taxol in this Taxol-dependent cell line. In A549-T12 cells, the presence of Taxol significantly amplified the cytotoxicity of discodermolide, and this phenomenon was not obsd. in combinations of Taxol with either the epothilones or eleutherobin. Median effect anal. using the combination index method revealed a schedule-independent synergistic interaction between Taxol and discodermolide in four human carcinoma cell lines, an effect that was not obsd. between Taxol and epothilone B. Flow cytometry revealed that concurrent exposure of A549 cells to Taxol and discodermolide at doses that do not induce mitotic arrest caused an increase in the hypodiploid population, thereby indicating that a possible mechanism for the obsd. synergy is the potentiation of apoptosis. Our results suggest that Taxol and discodermolide may constitute a promising chemotherapeutic combination.

IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(taxol and discodermolide represent a synergistic drug combination in human carcinoma cell lines)

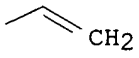
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

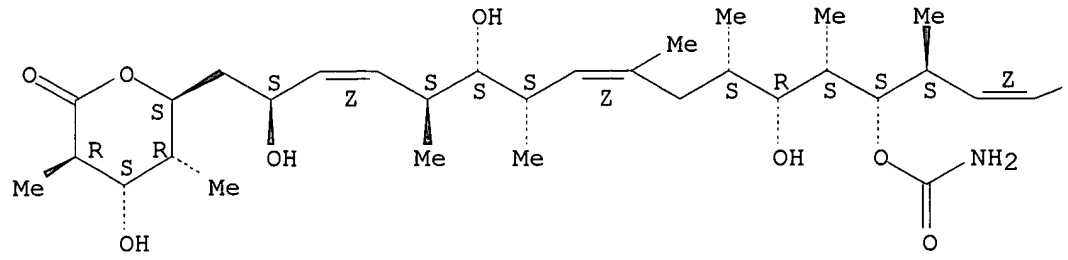


REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

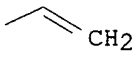
L4 ANSWER 54 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:304846 CAPLUS
DOCUMENT NUMBER: 133:43338
TITLE: An efficient gram-scale synthesis of (+)-discodermolide
AUTHOR(S): Nair, Sajiv K.; Henri, John T.; Georg, Gunda I.
CORPORATE SOURCE: University of Kansas, USA
SOURCE: Chemtracts (2000), 13(4), 229-236
CODEN: CHEMFW; ISSN: 1431-9268
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The title research of A.B. Smith III, M.D. Kaufman, T.J. Beauchamp, M.J. LaMarche and H. Arimoto (1999) is reviewed with commentary and 28 refs.
IT **127943-53-7P**, (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(efficient gram-scale synthesis of (+)-discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

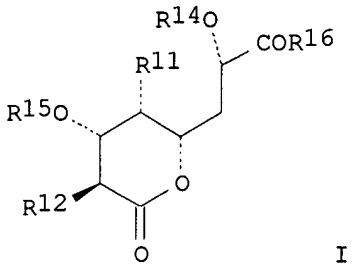


REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

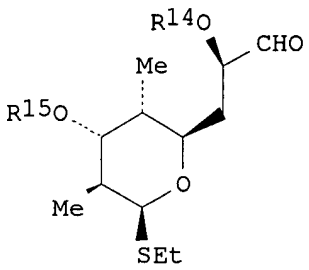
L4 ANSWER 55 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:84572 CAPLUS
DOCUMENT NUMBER: 132:137207
TITLE: Preparation of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone derivatives for pharmaceutical use
INVENTOR(S): Smith, Amos B. Iii; Qiu, Yuping; Kaufman, Michael; Arimoto, Hirokazu; Jones, David R.; Kobayashi, Kaoru; Beauchamp, Thomas J.
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004865	A2	20000203	WO 1999-US16369	19990720
WO 2000004865	A3	20000921		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6096904	A	20000801	US 1998-121551	19980723
AU 9952190	A1	20000214	AU 1999-52190	19990720
AU 749844	B2	20020704		
EP 1105383	A2	20010613	EP 1999-937330	19990720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002521317	T2	20020716	JP 2000-560858	19990720

PRIORITY APPLN. INFO.: US 1998-121551 A 19980723
US 1996-759817 A2 19961203
WO 1999-US16369 W 19990720
OTHER SOURCE(S): MARPAT 132:137207
GI



I



II

AB Prepn. of intermediates, such as I [R11, R12 = alkyl; R14, R15 = acid labile protecting groups; R16 = H, alkyl], for the synthesis of discodermolides and their analogs, which are useful as pharmaceuticals, was presented. Thus, synthon II (R14 = R15 = SiMe2CMe3) was prepd. via a multistep synthetic sequence starting from (2R)-3-hydroxy-2-methylpropanoic acid Me ester. The synthetic utility of II was subsequently demonstrated by its use in the prepn. of (-)-discodermolide.

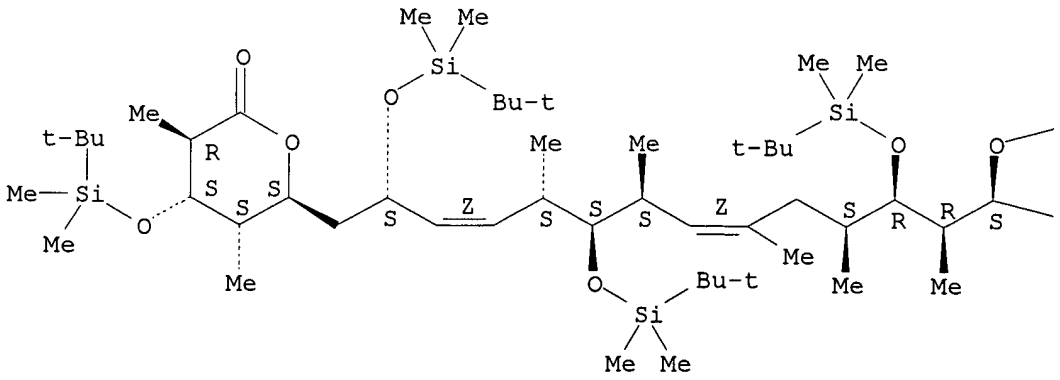
IT **252342-55-5 256921-06-9 256921-63-8 256921-65-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of intermediates for the synthesis of discodermolides and their polyhydroxy dienyl lactone derivs. for pharmaceutical use)

RN 252342-55-5 CAPLUS

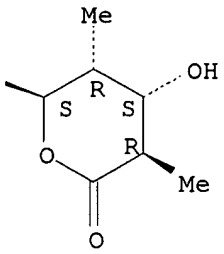
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



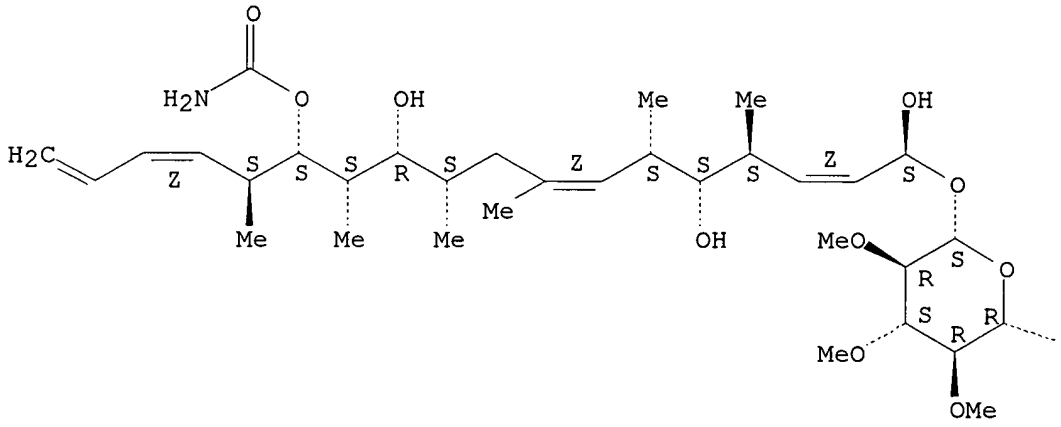
PAGE 1-B



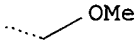
RN 256921-48-9 CAPLUS
CN .beta.-D-Glucopyranoside, (1S,2Z,4S,5S,6S,7Z,10S,11R,12S,13S,14S,15Z)-13-[(aminocarbonyl)oxy]-1,5,11-trihydroxy-4,6,8,10,12,14-hexamethyl-2,7,15,17-octadecatetraenyl 2,3,4,6-tetra-O-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 56 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:76529 CAPLUS

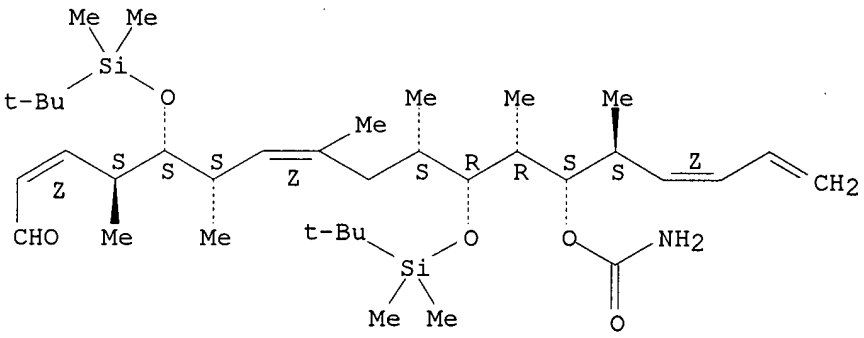
DOCUMENT NUMBER: 132:236926
TITLE: Total synthesis of the antimicrotubule agent (+)-discodermolide using boron-mediated aldol reactions of chiral ketones
AUTHOR(S): Paterson, Jan; Florence, Gordon J.; Gerlach, Kai; Scott, Jeremy
CORPORATE SOURCE: Univ. Chem. Lab., Cambridge, CB2 1EW, UK
SOURCE: Angewandte Chemie, International Edition (2000), 39(2), 377-380
CODEN: ACIEF5; ISSN: 1433-7851
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The total synthesis of (+)-discodermolide is achieved in 27 steps in 7.7% yield staring from Me (S)-3-hydroxy-2-methylpropionate. The three key subunits were prepd. using boron-mediated anti-selective aldol reactions.

IT **261968-08-5P 261968-24-5P 261968-25-6P 261968-26-7P 261968-27-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (+)-discodermolide via boron-mediated aldol reactions of chiral ketones)

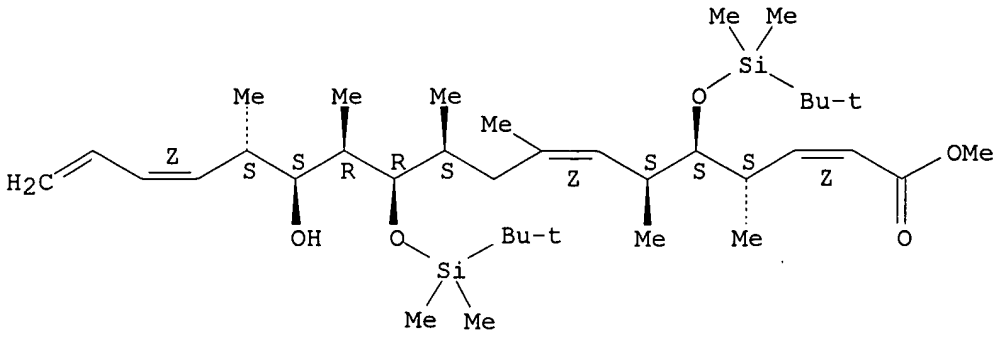
RN 261968-08-5 CAPLUS
CN 2,7,15,17-Octadecatetraenal, 13-[(aminocarbonyl)oxy]-5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-4,6,8,10,12,14-hexamethyl-, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



RN 261968-24-5 CAPLUS
CN 2,7,15,17-Octadecatetraenoic acid, 5,11-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-13-hydroxy-4,6,8,10,12,14-hexamethyl-, methyl ester, (2Z,4S,5S,6S,7Z,10S,11R,12R,13S,14S,15Z)- (9CI) (CA INDEX NAME)

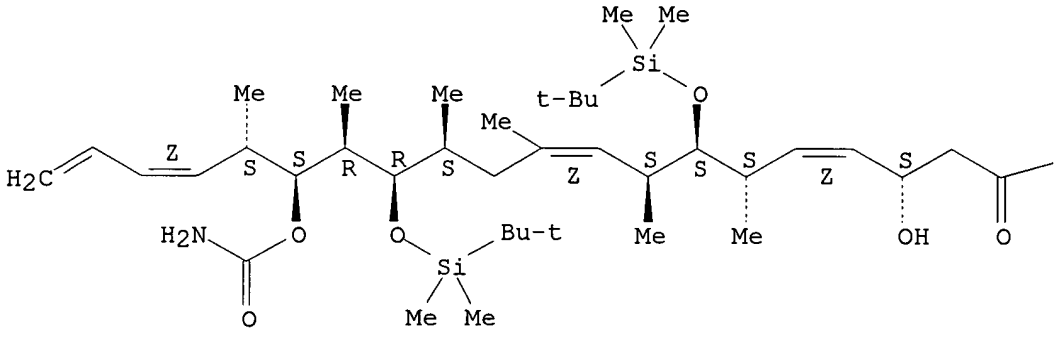
Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



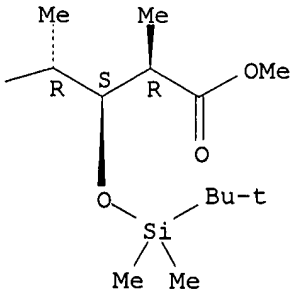
RN 261968-25-6 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-5-oxo-, methyl ester, (2R,3S,4R,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

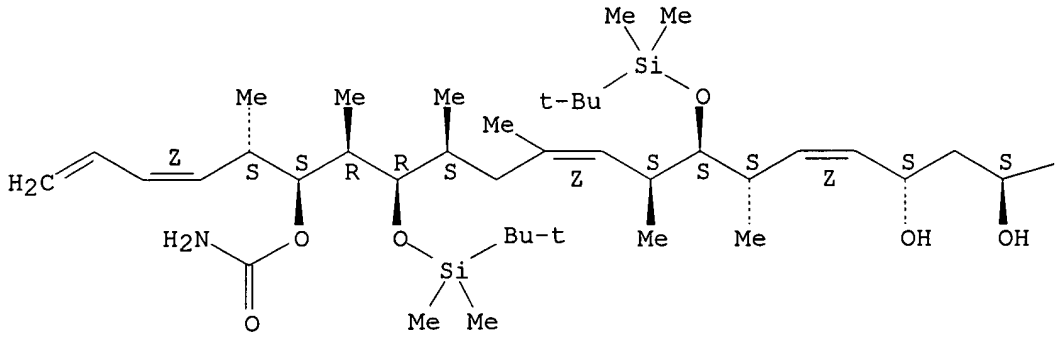


RN 261968-26-7 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-3,11,17-

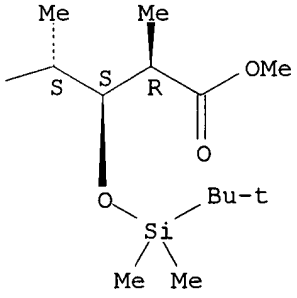
tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7-dihydroxy-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4S,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



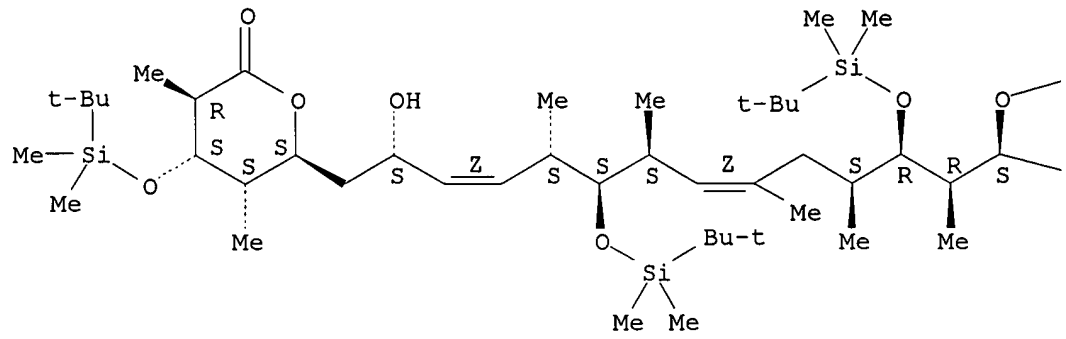
PAGE 1-B



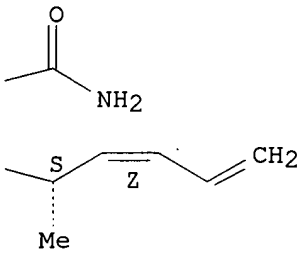
RN 261968-27-8 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-6,12-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



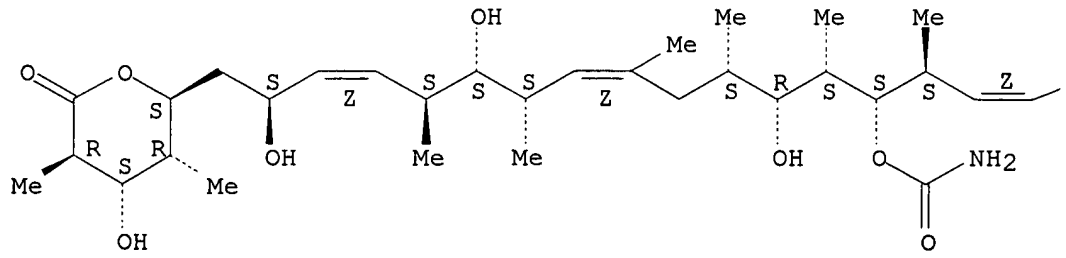
PAGE 1-B

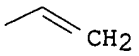


IT **127943-53-7P**, (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (+)-discodermolide via boron-mediated aldol reactions of chiral ketones)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:783929 CAPLUS
DOCUMENT NUMBER: 132:18780
TITLE: Compositions comprising antimicrotubule agents for treating or preventing inflammatory diseases
INVENTOR(S): Hunter, William L.
PATENT ASSIGNEE(S): Angiotech Pharmaceuticals, Inc., Can.
SOURCE: PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962510	A2	19991209	WO 1999-CA464	19990601
WO 9962510	A3	20000406		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9940255	A1	19991220	AU 1999-40255	19990601

PRIORITY APPLN. INFO.:
US 1998-88546P P 19980601
US 1998-88546 A 19980601
WO 1999-CA464 W 19990601

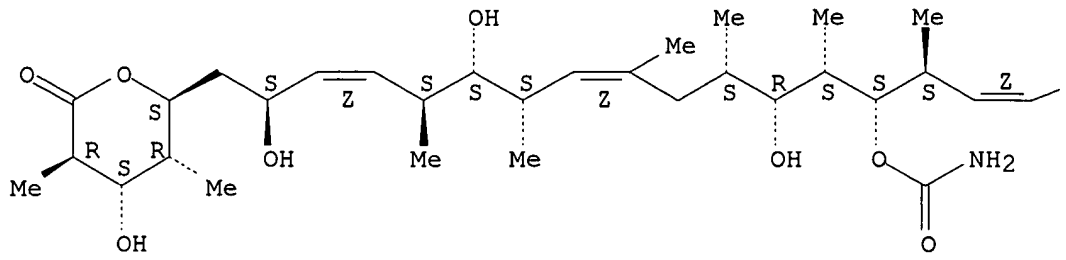
AB Methods and compns. for treating or preventing inflammatory diseases, e.g. psoriasis or multiple sclerosis, are provided, comprising the step of delivering to the site of inflammation an antimicrotubule agent, or analog or deriv. thereof.

IT **127943-53-7 127943-53-7D**, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antimicrotubule agents for treating or preventing inflammatory diseases)

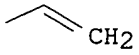
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



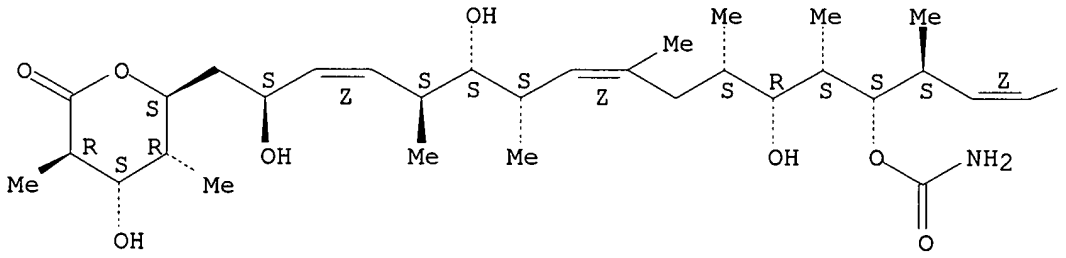
PAGE 1-B



RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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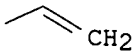


L4 ANSWER 58 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:694867 CAPLUS
DOCUMENT NUMBER: 132:35548
TITLE: Gram-Scale Synthesis of (+)-Discodermolide
AUTHOR(S): Smith, Amos B., III; Kaufman, Michael D.; Beauchamp, Thomas J.; LaMarche, Matthew J.; Arimoto, Hirokazu
CORPORATE SOURCE: Department of Chemistry Monell Chemical Senses Center and Laboratory for Research on the Structure of

Matter, University of Pennsylvania, PA, 19104, USA
SOURCE: Organic Letters (1999), 1(11), 1823-1826
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A triply convergent, highly efficient second-generation synthesis of the potent antimitotic agent (+)-discodermolide has been achieved on a 1-g scale.

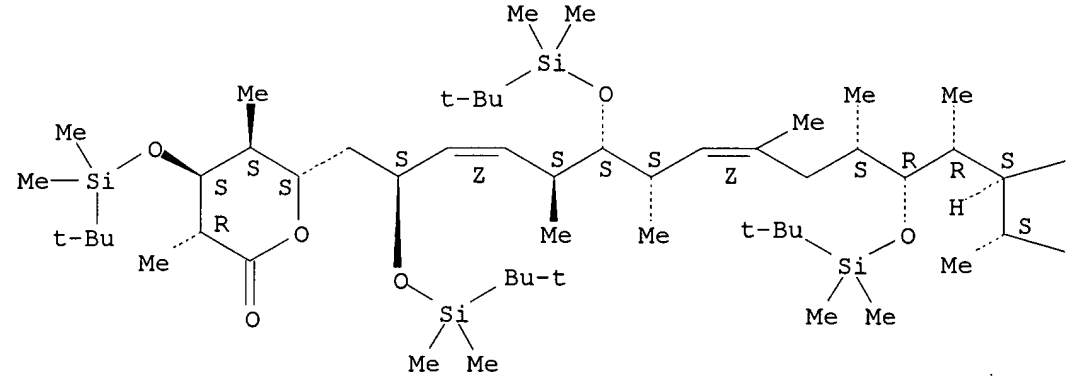
IT **252342-47-5P 252342-48-6P 252342-55-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(gram-scale synthesis of (+)-discodermolide)

RN 252342-47-5 CAPLUS

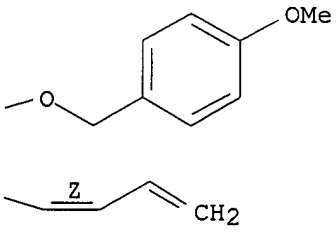
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

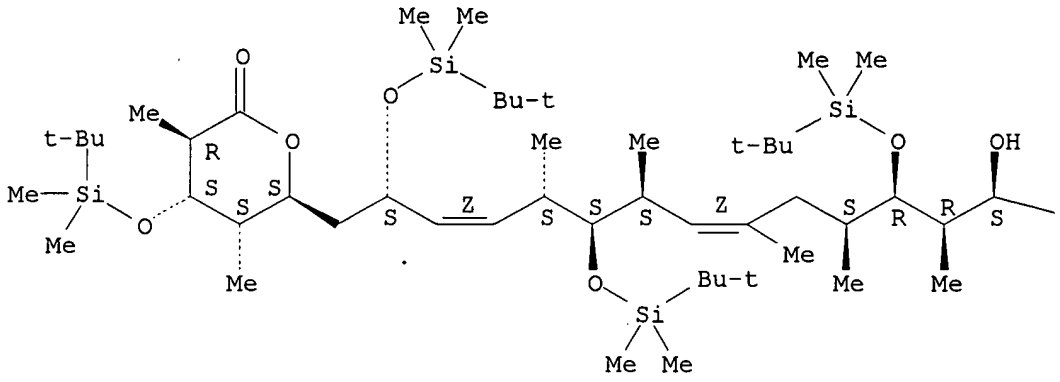


RN 252342-48-6 CAPLUS

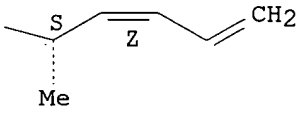
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



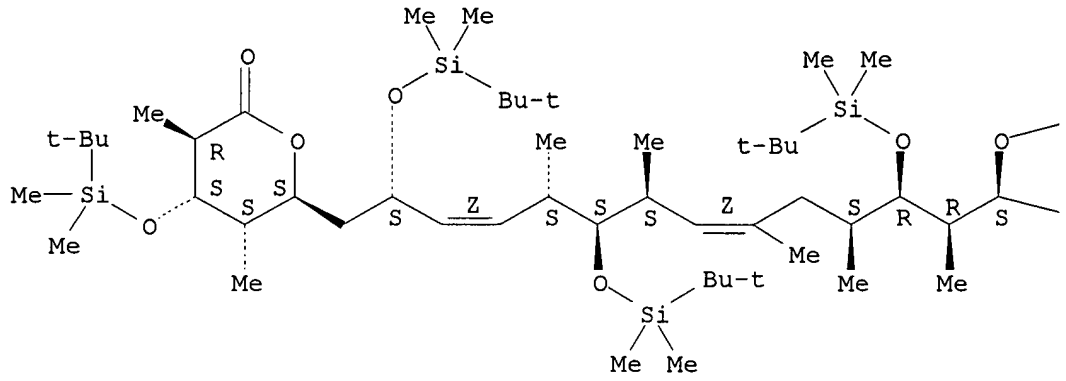
PAGE 1-B



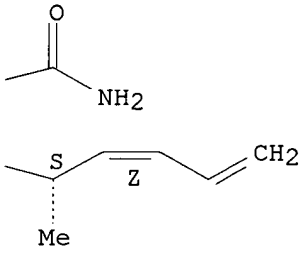
RN 252342-55-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13R,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3R,4S,5S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



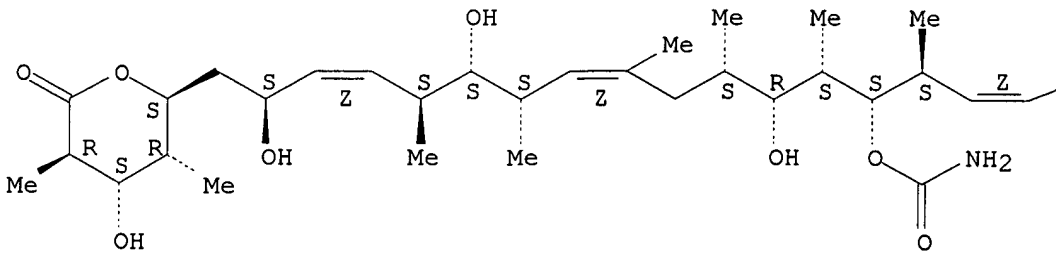
PAGE 1-B



IT **127943-53-7P**, (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(gram-scale synthesis of (+)-discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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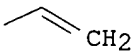
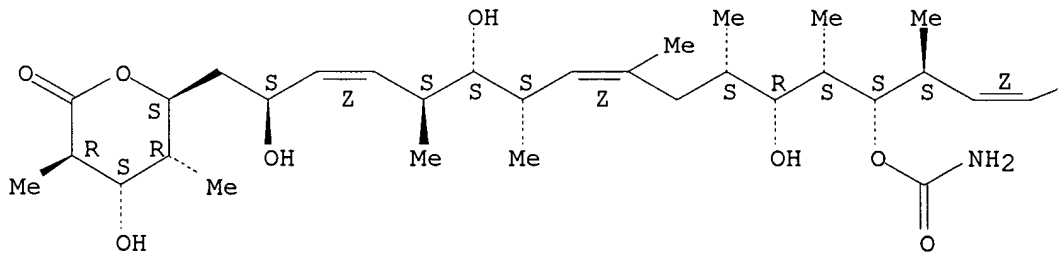


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

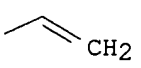
L4 ANSWER 59 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:567611 CAPLUS
DOCUMENT NUMBER: 132:194227
TITLE: Total synthesis of (+)-miyakolide. I. Total synthesis of (-)-discodermolide. II. Total synthesis of (+)-discodermolide
AUTHOR(S): Halstead, David Patrick
CORPORATE SOURCE: Harvard Univ., Cambridge, MA, USA
SOURCE: (1999) 199 pp. Avail.: UMI, Order No. DA9921509 From: Diss. Abstr. Int., B 1999, 60(3), 1087
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7P**, (+)-Discodermolide **154335-30-5P**, (-)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

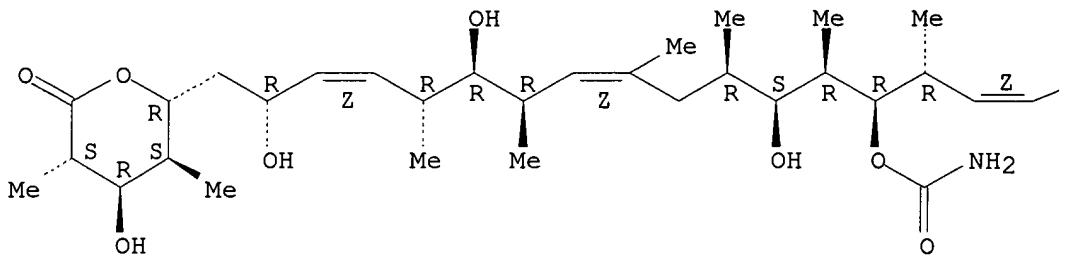


RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-

[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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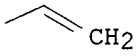


L4 ANSWER 60 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:483464 CAPLUS
DOCUMENT NUMBER: 132:127501
TITLE: Forward position of study on marine drugs abroad and a strategy of development of marine drugs in China
AUTHOR(S): Fan, Xiao; Yan, Xiaojun; Du, Guanhua; Shi, Jiangong
CORPORATE SOURCE: Institute of Oceans, Chinese Academy of Sciences, Tsingtao, 266071, Peop. Rep. China
SOURCE: Zhongguo Haiyang Yaowu (1999), 18(2), 42-45
CODEN: ZHYAE8; ISSN: 1002-3461
PUBLISHER: Shandongsheng Haiyang Yaowu Kexue Yanjiuso
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Chinese

AB A review with 10 refs. on forward position of study on marine drugs abroad and a strategy of development of marine drugs in China with subdivision headings: the marine drugs entered and would be entered into the clin. usage including didemnin B, bryostatin, dolastatin 10, discodermolide, manoalide and halomon; the strategy of development of marine drugs in China and summary.

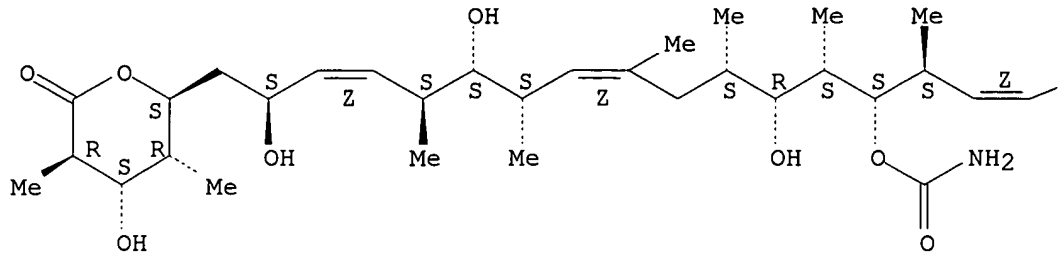
IT **127943-53-7**, Discodermolide
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(marine drugs in China and elsewhere)

RN 127943-53-7 CAPLUS

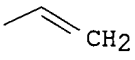
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

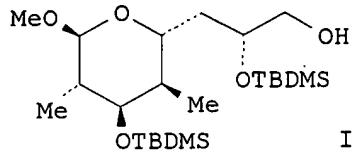


PAGE 1-B

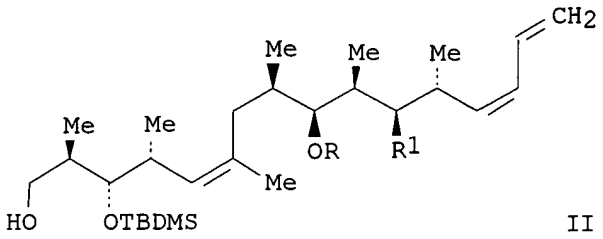


L4 ANSWER 61 OF 111 CAPLUS COPYRIGHT 2002 ACS

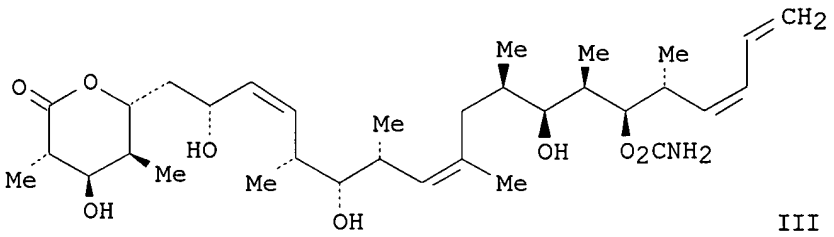
ACCESSION NUMBER: 1999:461996 CAPLUS
DOCUMENT NUMBER: 131:271758
TITLE: Synthesis of C1-C8 and C9-C24 fragments of (-)-discodermolide: use of asymmetric alkylation and stereoselective aldol reactions
AUTHOR(S): Filla, Sandra A.; Song, Jinhua J.; Chen, Lihren; Masamune, Satoru
CORPORATE SOURCE: Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA
SOURCE: Tetrahedron Letters (1999), 40(30), 5449-5453
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:271758
GI



I



II



III

AB The C1-C8 fragment I (TBDMS = SiMe2CMe3) and C9-C24 fragment II (R = TBDMS; R1 = CH2C6H4OMe-4) of (-)-discodermolide (III), the antipode of the marine natural product (+)-discodermolide, have been synthesized with excellent stereoselectivities. These syntheses feature the utilization of the isoxazolidine-mediated asym. alkylation methodol. and fragment-fragment coupling aldol reactions.

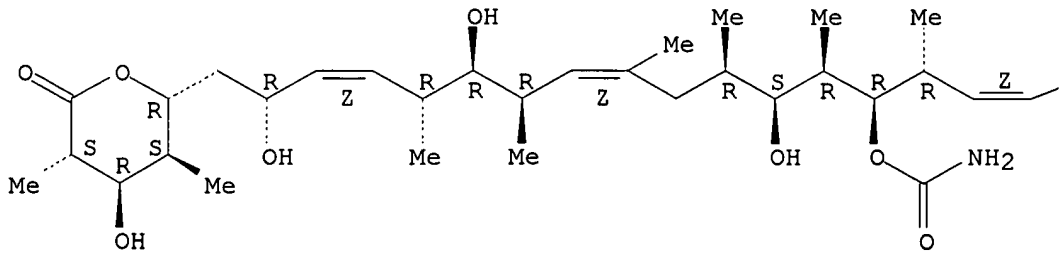
IT **154335-30-5P**, (-)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of C1-C8 and C9-C24 fragments of (-)-discodermolide via asym. alkylation and stereoselective aldol reactions)

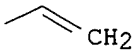
RN 154335-30-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 62 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:368580 CAPLUS
DOCUMENT NUMBER: 131:164976
TITLE: A common pharmacophore for cytotoxic natural products that stabilize microtubules
AUTHOR(S): Ojima, Iwao; Chakravarty, Subrata; Inoue, Tadashi; Lin, Songnian; He, Lifeng; Horwitz, Susan Band; Kuduk, Scott D.; Danishefsky, Samuel J.
CORPORATE SOURCE: Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY, 11794-3400, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1999), 96(8), 4256-4261
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

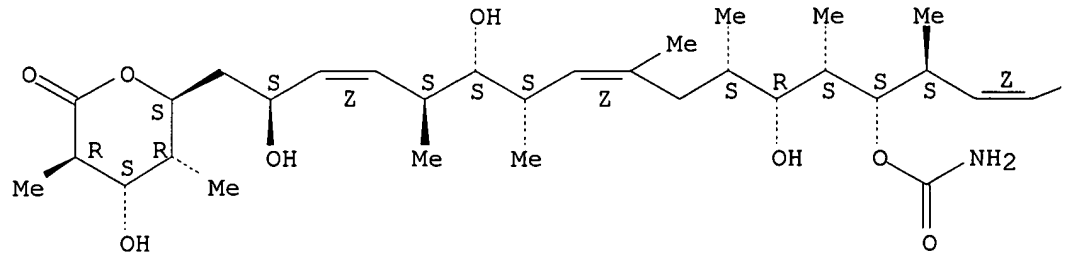
AB Paclitaxeltaxol (paclitaxel), a complex diterpene obtained from the Pacific yew, Taxus brevifolia, is arguably the most important new drug in cancer chemotherapy. The mechanism of cytotoxic action for paclitaxel-i.e., the stabilization of microtubules leading to mitotic arrest-is now shared by four recently identified natural products, eleutherobin, epothilones A and B, and discodermolide. Their ability to competitively inhibit [3H]paclitaxel binding to microtubules strongly suggests the existence of a common binding site. Recently, the authors have developed nonarom. analogs of paclitaxel that maintain high cytotoxicity and tubulin binding (e.g., nonataxel). The authors now propose a common pharmacophore that unites paclitaxel, nonataxel, the epothilones, eleutherobin, and discodermolide, and rationalizes the extensive structure-activity relation data pertinent to these compds. Insights from the common pharmacophore have enabled the development of a hybrid construct with demonstrated cytotoxic and tubulin-binding activity.

IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(common pharmacophore for cytotoxic natural products that stabilize microtubules)

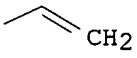
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 63 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:363548 CAPLUS
DOCUMENT NUMBER: 131:129557
TITLE: Chelation-controlled stannylacetylene additions to .beta.-alkoxy aldehydes promoted by alkylaluminum halide Lewis acids
AUTHOR(S): Evans, David A.; Halstead, David P.; Allison, Brett D.
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Tetrahedron Letters (1999), 40(24), 4461-4462
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:129557
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

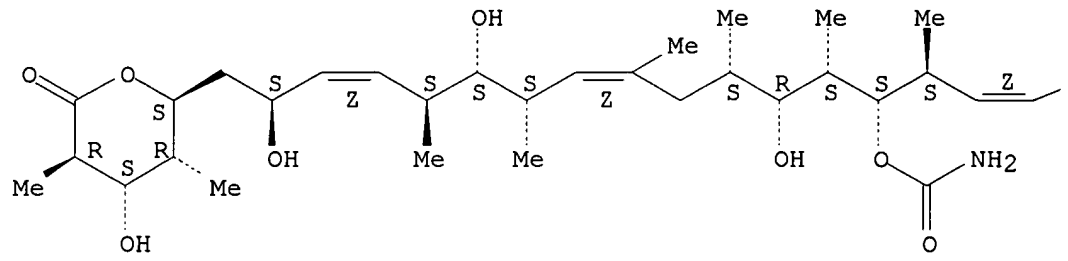
AB Lewis acid-mediated stereoselective addns. of stannylacetylenes RC.tplbond.CSnMe3 [R = Ph, t-BuPh2SiO(CH2)4] to .beta.-alkoxy aldehydes (I and II; wherein R1 = CH2Ph, t-BuMe2Si) to give Felkin or anti-Felkin adducts (1,3-syn-III, 1,3-anti-IV, 1,3-syn-V, or 1,3-anti-VI) are reported. High levels of chelation control are obsd. with dimethylaluminum chloride (Me2AlCl) and methylaluminum dichloride (MeAlCl2). Thus, aldehyde (VII) underwent addn. reaction with stannylacetylene deriv. (VIII; R = SnMe3) in the presence of 5 equiv of MeAlCl2 in toluene at -78.degree. to give VIII (R = Q) with anti/syn diastereoselection of 82/18 which is an intermediate for discodermolide.

IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(chelation-controlled stannylacetylene addns. to .beta.-alkoxy aldehydes promoted by alkylaluminum halide Lewis acids)

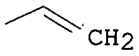
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:359469 CAPLUS
DOCUMENT NUMBER: 131:153512
TITLE: Increased sensitivity of the antiestrogen-resistant MCF-7/LY2 human breast carcinoma cell line to apoptosis induced by the novel microtubule stabilizing agent (+)-discodermolide
AUTHOR(S): Balachandran, Raghavan; Grant, Stephen G.; Welsh, Manda J.; Day, Billy W.
CORPORATE SOURCE: Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, 15238, USA
SOURCE: Breast Journal (1998), 4(6), 409-419
CODEN: BRJOFK; ISSN: 1075-122X
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (+)-Discodermolide is a sponge-derived natural product with the most potent microtubule-stabilizing activity yet discovered. Its actions parallel that of the promising anti-breast cancer agent paclitaxel despite the lack of any apparent similarities in the drugs' structures. To complement previous studies on human breast cancer cells, the authors compared the effects of the 2 drugs against the estrogen receptor-pos. but tamoxifen-resistant MCF-7/LY2 line. Growth inhibition, cell, and nuclear morphol., electrophoretic, and flow cytometric analyses were performed. (+)-Discodermolide potently inhibited the growth of the cells (e.g., 48-h IC50 of 1.5 nM) at concns. similar to those obsd. with paclitaxel, and somewhat lower than the values obsd. previously with estrogen-responsive MCF-7 cells and estrogen-nonresponsive MDA-MB231 cells.

(+)-Discodermolide-treated MCF-7/LY2 cells had condensed and highly fragmented nuclei, as well as micronuclei, suggesting mitotic block and the induction of apoptosis. Flow cytometric comparison of cells treated with either drug at 10 nM showed both caused the accumulation into the G2/M portion of the cell cycle as well as the induction of a pronounced hypodiploid cell population, with (+)-discodermolide yielding a greater effect. The timing and type of high mol. wt. DNA fragmentation induced by the 2 agents was fully consistent with the induction of apoptosis, again with (+)-discodermolide showing an advantage over paclitaxel in this regard. More extensive DNA fragmentation was noted in MCF-7/LY2 than has been obsd. in MCF-7 and MDA-MB231 cells. These in vitro results, coupled with those obtained previously, suggest that (+)-discodermolide might have promise as a new chemotherapeutic agent against breast cancers. In addn., its novel and synthetically approachable structure make (+)-discodermolide a promising lead compd. for the design and discovery of new microtubule-stabilizing agents as alternatives to taxoids.

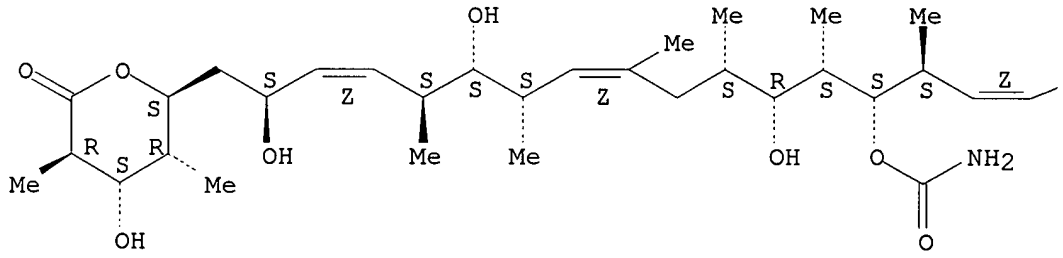
IT **127943-53-7**, (+)-Discodermolide
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(increased sensitivity of antiestrogen-resistant MCF-7/LY2 human breast carcinoma cell line to apoptosis induced by (+)-discodermolide)

RN 127943-53-7 CAPLUS

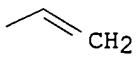
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



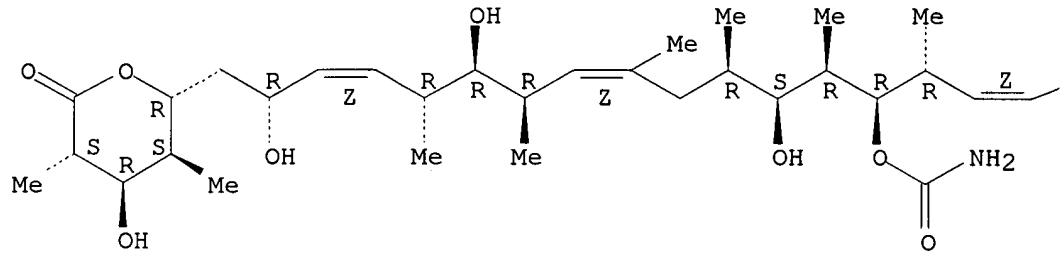
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 65 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:320599 CAPLUS
DOCUMENT NUMBER: 131:199544
TITLE: A total synthesis of (-)-discodermolide
AUTHOR(S): Harried, Scott S.
CORPORATE SOURCE: Univ. of California, Los Angeles, CA, USA
SOURCE: (1998) 189 pp. Avail.: UMI, Order No. DA9913066

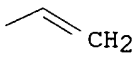
From: Diss. Abstr. Int., B 1999, 59(11), 5854
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **154335-30-5P**, (-)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-discodermolide)
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

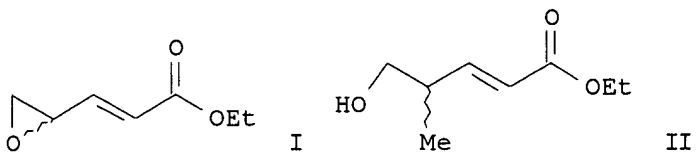
PAGE 1-A

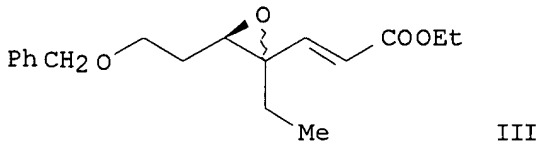


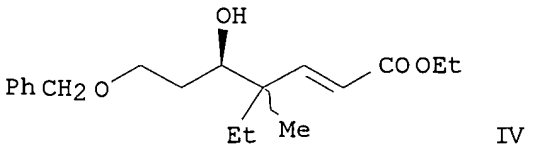
PAGE 1-B



L4 ANSWER 66 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:286766 CAPLUS
DOCUMENT NUMBER: 131:129813
TITLE: Natural product synthesis based on the stereospecific acyclic stereocontrol
AUTHOR(S): Miyazawa, Masahiro; Maruyama, Kimiyuki; Sasaki, Shinobu; Ohnuma, Satoshi; Ishibashi, Naoki; Sasaki, Minoru; Miyashita, Masaaki
CORPORATE SOURCE: Graduate School of Science, Hokkaido University, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1998), 40th, 211-216
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
GI







AB The authors recently developed a novel acyclic stereocontrol based on the stereospecific methylation of .gamma.,.delta.-epoxy acrylates with trimethylaluminum in the presence of water by which both anti and syn compds. can be highly stereoselectively synthesized from trans- and cis-.gamma.,.delta.-epoxy acrylates, resp. The authors report here stereospecific internal alkylation of terminal epoxides and stereospecific construction of asym. quaternary carbons via .gamma.,.delta.-epoxy acrylates. The authors also report synthetic studies toward total synthesis of a marine natural product discodermolide and epothilone based on the above methodologies. Regio- and stereoselective internal alkylation of terminal epoxides has little been known. The authors designed such a reaction using .gamma.,.delta.-epoxy acrylates with trimethylaluminum. The reaction of terminal .gamma.,.delta.-epoxy acrylates (S)- and (R)-I, easily prepd. from D-mannitol, with excess trimethylaluminum in the presence of water proceeded regiospecifically at the .gamma.-position to give (R)- and (S)-II, as the sole product, resp., with maintenance of optical integrity. Regarding stereospecific construction of asym. quaternary carbons via .gamma.-Alkyl-.gamma.,.delta.-epoxy acrylates, the authors found that the reaction of .gamma.-alkyl-.gamma.,.delta.-epoxy acrylates with trialkylaluminum and water occurs regio- and stereo-specifically at the .gamma.-position as well yielding an asym. quaternary carbon. Thus, treatment of (4R)- and (4S)-III with excess trimethylaluminum in the presence of water gave (4R)- and (4S)-IV as a single product, resp., in which a Me group was stereospecifically introduced at the .gamma.-position with net inversion of configuration. Regarding synthetic studies on discodermolide and epothilone, the authors set out synthesis of discodermolide having potent immunosuppressive activity based on the above stereospecific acyclic stereocontrol. Discodermolide was divided into three segments in which the segment B having three contiguous chiral centers and the segment C possessing five chiral centers have been highly stereoselectively synthesized. Stereoselective synthesis of the C1-C9 segment of epothilone having potent anticancer activity was also carried out in which five asym. centers was highly stereoselectively constructed by repeating the above methylation reaction.

IT **127943-53-7P**, Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)

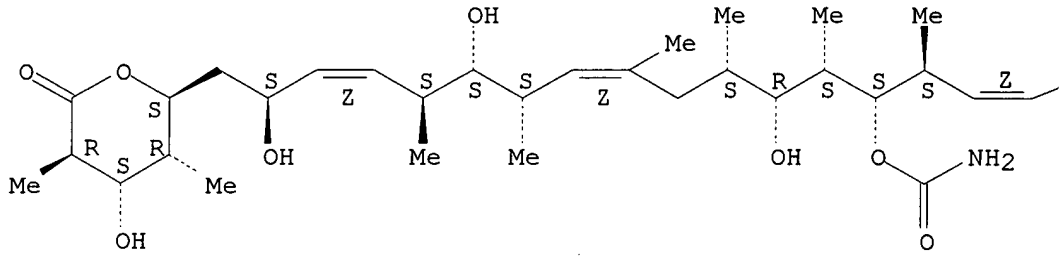
(natural product synthesis based on stereospecific acyclic stereocontrol)

RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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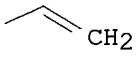


L4 ANSWER 67 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:256009 CAPLUS

DOCUMENT NUMBER: 131:44692

TITLE: Asymmetric synthesis of seven-carbon segments of the phorboxazoles and (-)-discodermolide: complementary route from racemic trans-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one

AUTHOR(S): Misske, Andrea M.; Hoffmann, H. M. R.

CORPORATE SOURCE: Department of Organic Chemistry, University of Hannover, Hannover, D-30167, Germany

SOURCE: Tetrahedron (1999), 55(14), 4315-4324
CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 131:44692

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The C20-C26 segment of the phorboxazoles A (I; R = .alpha.-OH) and B (I; R = .beta.-OH) and the C1-C7 segment of (-)-discodermolide (II) were synthesized in excellent chem. and optical yield using trans-2,4-dimethyl-8-oxabicyclo[3.2.1]oct-6-en-3-one rac-III with four stereogenic centers and three prostereogenic sp2-sites as an early racemic

switch.

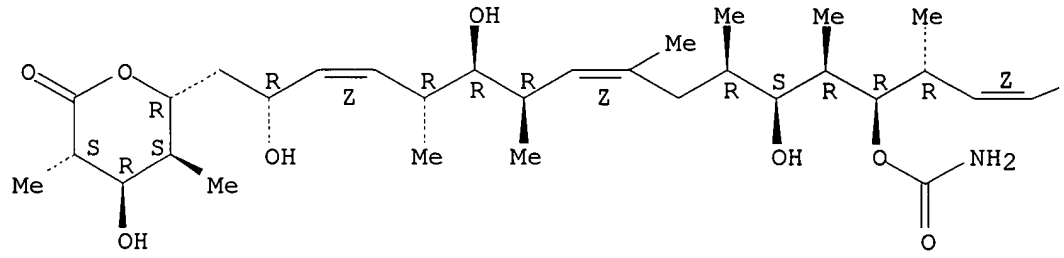
IT **154335-30-5P**, (-)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(asym. synthesis of the dimethylpyranol segments of the phorboxazoles and (-)-discodermolide)

RN 154335-30-5 CAPLUS

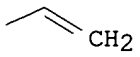
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:213344 CAPLUS
DOCUMENT NUMBER: 131:31646
TITLE: A Density Functional Study of a New Family of Anticancer Drugs: Paclitaxel, Taxotere, Epothilone, and Discodermolide
AUTHOR(S): Ballone, P.; Marchi, M.
CORPORATE SOURCE: Institut fuer Festkoerperforschung, Forschungszentrum Juelich, Juelich, D-52425, Germany
SOURCE: Journal of Physical Chemistry A (1999), 103(16), 3097-3102
CODEN: JPCAFH; ISSN: 1089-5639
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We present a d.-functional study of the paclitaxel, taxotere, baccatin III, epothilone-A, and discodermolide mols. in their gas phase. For each of these compds. we det. the geometry and the electronic structure of the ground state and of some isomers and analogs. We find that the central part of all these mols. is insensitive to changes in structure, orientation, and isomerization of its tail and is characterized by a rather large dipole that has similar orientation with respect to the mol. frame. These similarities extend also to the electronic structure. Our

results provide an extended and consistent set of data to gauge classical force fields in view of the atomistic investigations of the interaction of these mols. with tubulin.

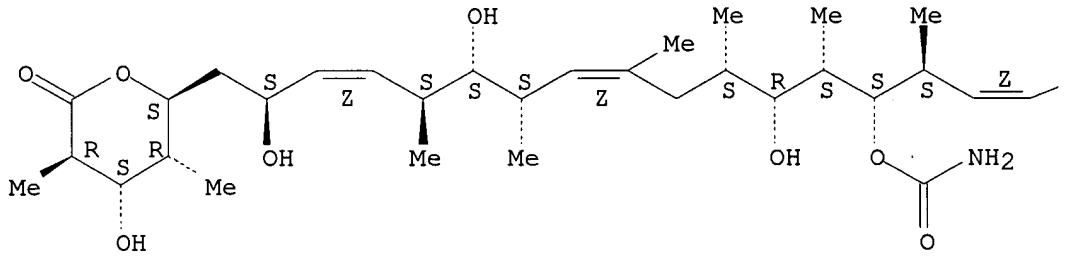
IT **127943-53-7**, Discodermolide
RL: PRP (Properties)
(d. functional study of family of anticancer drugs, paclitaxel, taxotere epothilone, and discodermolide)

RN 127943-53-7 CAPLUS

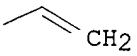
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 69 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:804132 CAPLUS
DOCUMENT NUMBER: 130:33009
TITLE: A method of treating cancer using an antineoplastic agent-prenyl-protein transferase inhibitor combination, and compound preparation
INVENTOR(S): Rosen, Neal; Sepp-lorenzino, Laura; Moasser, Mark M.; Oliff, Allen I.; Gibbs, Jackson B.; Kohl, Nancy; Graham, Samuel L.; Prendergast, George C.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Sloan-Kettering Institute for Cancer Research
SOURCE: PCT Int. Appl., 379 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854966	A1	19981210	WO 1998-US8646	19980604

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9877957	A1	19981221	AU 1998-77957	19980604
EP 986302	A1	20000322	EP 1998-926029	19980604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002503249	T2	20020129	JP 1999-502409	19980604

PRIORITY APPLN. INFO.: US 1997-48736P P 19970605
GB 1998-1231 A 19980121
WO 1998-US8646 W 19980604

AB Methods are provided for treating cancer using a combination of a compd. which is an antineoplastic agent and a compd. which is a inhibitor of prenyl-protein transferase. The methods comprise administering to a mammal, either sequentially in any order or simultaneously, amts. of .gtoreq.2 therapeutic agents selected from a compd. which is an antineoplastic agent and a compd. which is an inhibitor or prenyl-protein transferase. The invention also relates to methods of prepg. such compns.

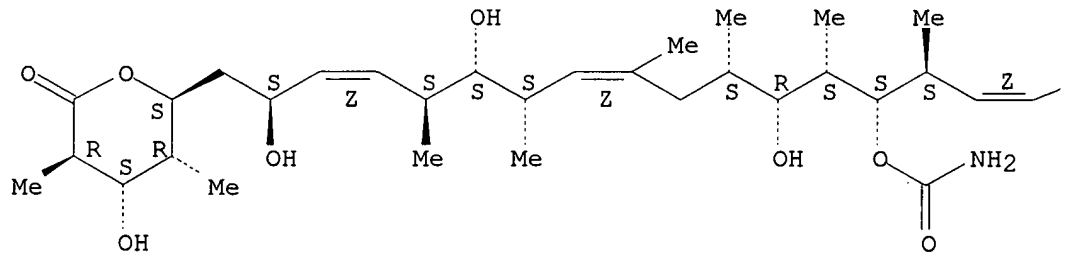
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antineoplastic agent-prenyl-protein transferase inhibitor combination for treating cancer, and compd. prepn.)

RN 127943-53-7 CAPLUS

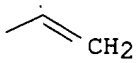
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1998:774245 CAPLUS
DOCUMENT NUMBER: 130:20558
TITLE: Discodermolide compounds useful for treatment of cancer
INVENTOR(S): Longley, Ross E.; Gunasekera, Sarath P.; Pomponi, Shirley A.
PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution Inc., USA
SOURCE: U.S., 31 pp., Cont.-in-part of U.S. Ser. No. 567,442.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840750	A	19981124	US 1996-761106	19961205
US 5681847	A	19971028	US 1995-567442	19951205
CA 2233716	AA	19970612	CA 1996-2233716	19961205

PRIORITY APPLN. INFO.: US 1995-567442 A2 19951205
OTHER SOURCE(S): MARPAT 130:20558

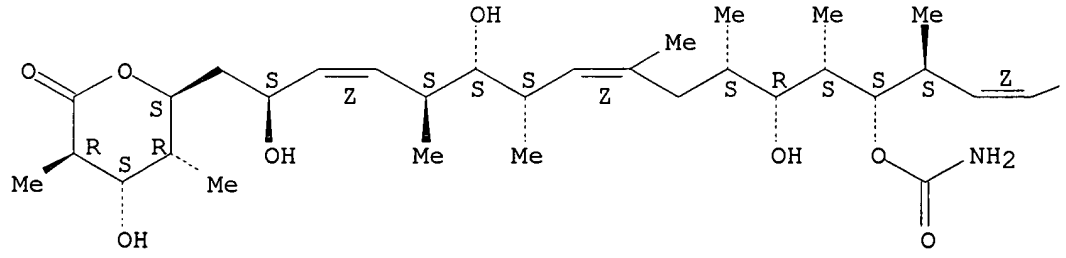
AB Lactone compds. from the marine sponge Discodermia dissoluta have been isolated. These compds. and their analogs have been shown to have activity against mammalian cancer cells, and can be used in treating human patients which host cancer cells, including leukemia, melanoma, and breast, colon, CNS, and lung tumors.

IT **127943-53-7D**, Discodermolide, derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discodermolide compds. useful for treatment of cancer)

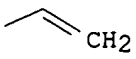
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



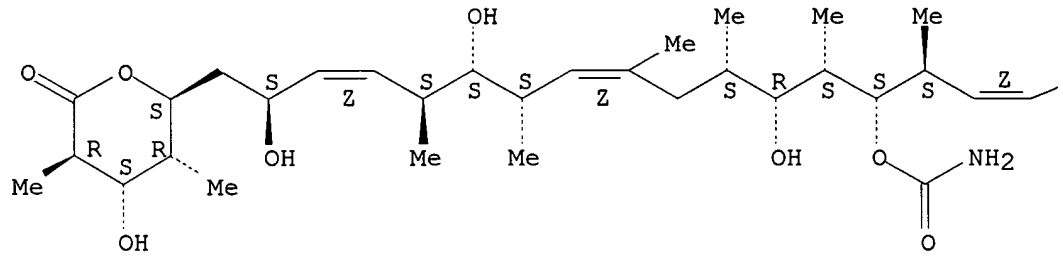
PAGE 1-B



IT **127943-53-7**, Discodermolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; discodermolide compds. useful for treatment of cancer)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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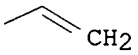

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 71 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:719255 CAPLUS
DOCUMENT NUMBER: 129:330604
TITLE: Synthesis of discodermolide and analogs via coupling of three chiral precursors
INVENTOR(S): Myles, David C.; Harried, Scott S.; Yang, Ge
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848791	A1	19981105	WO 1998-US8670	19980430

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9872672 A1 19981124 AU 1998-72672 19980430
PRIORITY APPLN. INFO.: US 1997-45215P P 19970430
WO 1998-US8670 W 19980430
OTHER SOURCE(S): CASREACT 129:330604
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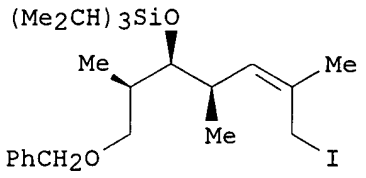

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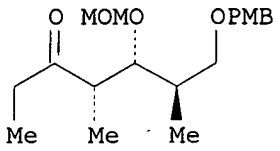

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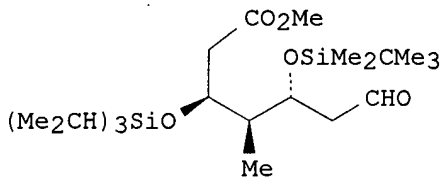
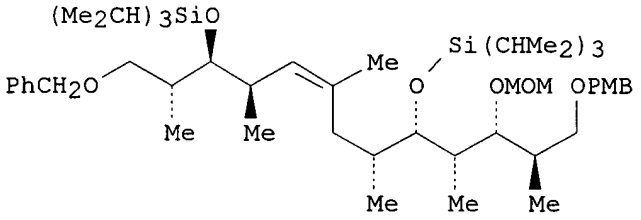


III



IV

AB A method for making discodermolide and its analogs utilizes three precursors - allylic iodide I, ketone II (MOM = CH2OMe; PMB = CH2C6H4OMe-4) and ester III - which correspond to three subparts of discodermolide which are formed by disconnecting the discodermolide carbon backbone at positions C-7 to C-8 and C-15 to C-16, and comprises chelation-controlled alkylation of precursors I and II to form the intermediate alkene IV. Thus, II is treated with LiN(SiMe3)2 in THF/hexane contg. TMEDA followed by addn. of I to give, after redn. with LiAlH4/LiI in ether and silylation with triisopropylsily triflate, intermediate IV. IV is converted to (-)-discodermolide via the following sequence: hydrogenolysis with H2 over Ra/Ni; oxidn. with TPAP/NMO; Wittig reaction with Ph3P:CHI; demethoxybenzylation with DDQ; a 2nd oxidn. with TPAP/NMO; allylation with [(E)-.gamma.-(trimethylsilyl)allyl]boron diisopropyl tartrate complex; demethoxmethylation with catecholborane chloride; acylation with Cl3CONCO; coupling with III in DMSO contg. CrCl2/NiCl2; and deprotection with HF.

IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of discodermolide and analogs via a chelation-controlled alkylation)

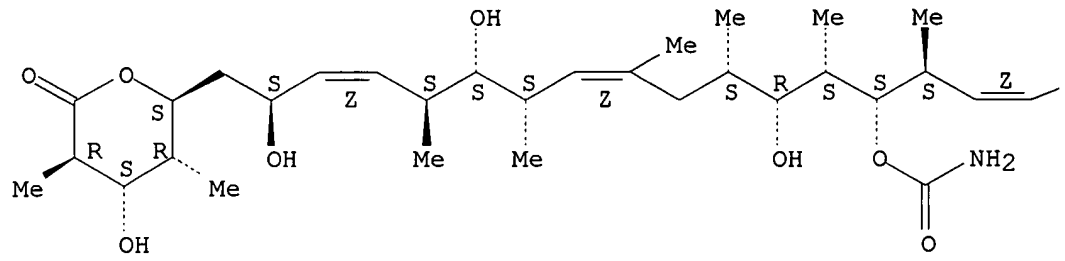
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI)

(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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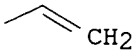
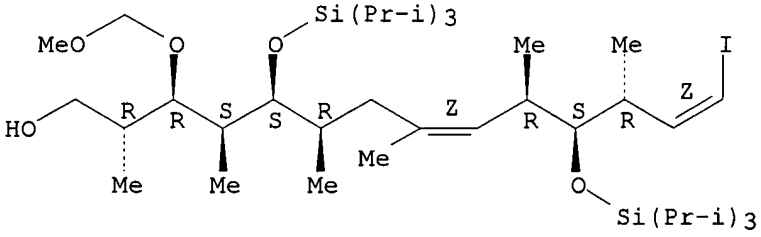


IT **194232-24-1P 194232-25-2P 194232-33-2P**
194232-34-3P 194232-35-4P 194232-36-5P
215106-13-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of discodermolide and analogs via a chelation-controlled alkylation)

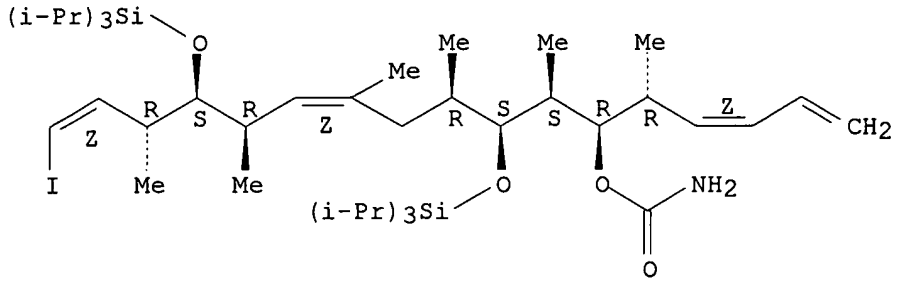
RN 194232-24-1 CAPLUS
CN 8,13-Tetradecadien-1-ol, 14-iodo-3-(methoxymethoxy)-2,4,6,8,10,12-hexamethyl-5,11-bis[[tris(1-methylethyl)silyl]oxy]-, (2R,3R,4S,5S,6R,8Z,10R,11S,12R,13Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



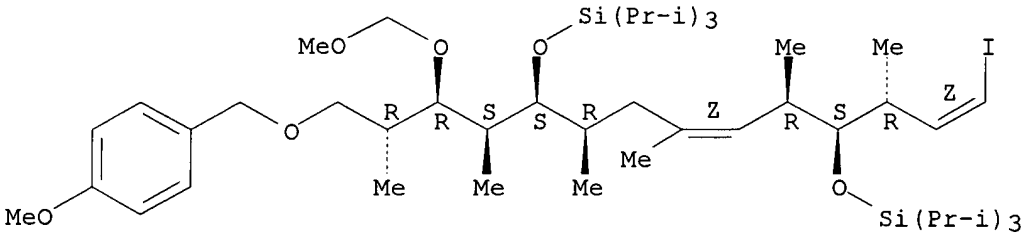
RN 194232-25-2 CAPLUS
CN 1,3,11,16-Heptadecatetraen-6-ol, 17-iodo-5,7,9,11,13,15-hexamethyl-8,14-bis[[tris(1-methylethyl)silyl]oxy]-, carbamate, (3Z,5R,6R,7S,8S,9R,11Z,13R,14S,15R,16Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



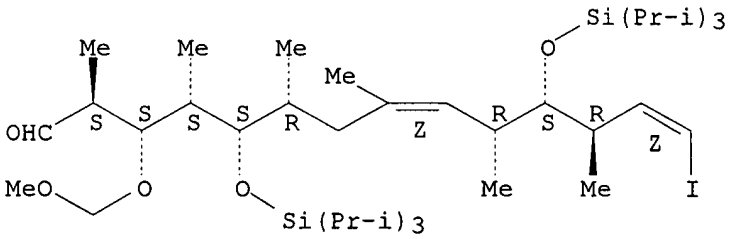
RN 194232-33-2 CAPLUS
CN 2,4,14-Trioxa-15-silaheptadec-10-ene, 13-[(1R,2Z)-3-iodo-1-methyl-2-propenyl]-5-[(1R)-2-[(4-methoxyphenyl)methoxy]-1-methylethyl]-6,8,10,12,16-pentamethyl-15,15-bis(1-methylethyl)-7-[[tris(1-methylethyl)silyl]oxy]-, (5R,6S,7S,8R,10Z,12R,13S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



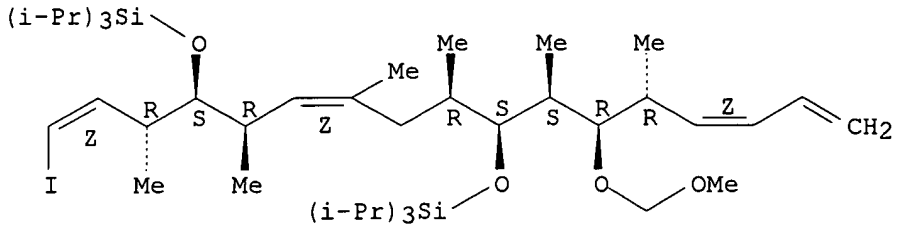
RN 194232-34-3 CAPLUS
CN 8,13-Tetradecadienal, 14-iodo-3-(methoxymethoxy)-2,4,6,8,10,12-hexamethyl-5,11-bis[[tris(1-methylethyl)silyl]oxy]-, (2S,3S,4S,5S,6R,8Z,10R,11S,12R,13Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



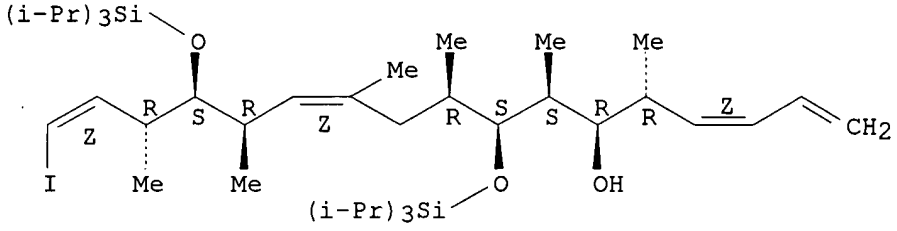
RN 194232-35-4 CAPLUS
CN 2,4,14-Trioxa-15-silaheptadec-10-ene, 13-[(1R,2Z)-3-iodo-1-methyl-2-propenyl]-6,8,10,12,16-pentamethyl-15,15-bis(1-methylethyl)-5-[(1R,2Z)-1-methyl-2,4-pentadienyl]-7-[[tris(1-methylethyl)silyl]oxy]-, (5R,6S,7S,8R,10Z,12R,13S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



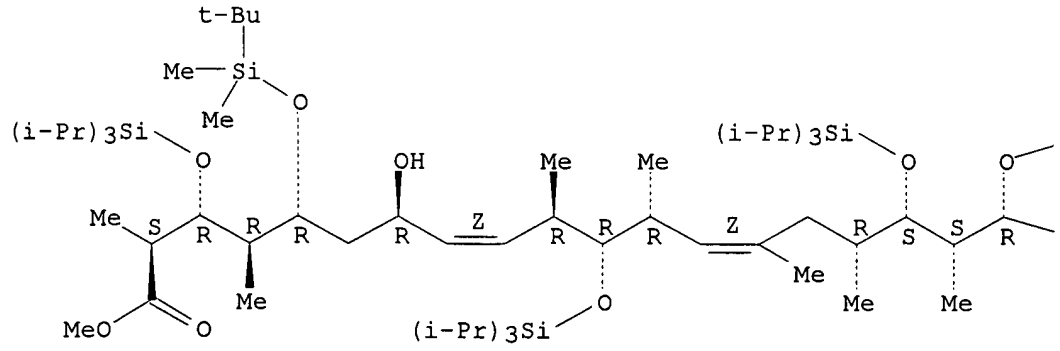
RN 194232-36-5 CAPLUS
CN 1,3,11,16-Heptadecatetraen-6-ol, 17-iodo-5,7,9,11,13,15-hexamethyl-8,14-bis[[tris(1-methylethyl)silyl]oxy]-, (3Z,5R,6R,7S,8S,9R,11Z,13R,14S,15R,16Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 215106-13-1 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-3,11,17-tris[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (2S,3R,4R,5R,7R,8Z,10R,11R,12R,13Z,16R,17S,18S,19R,20R,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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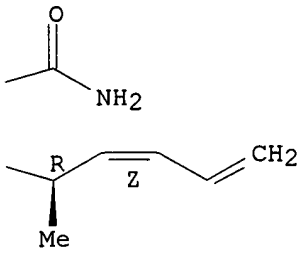


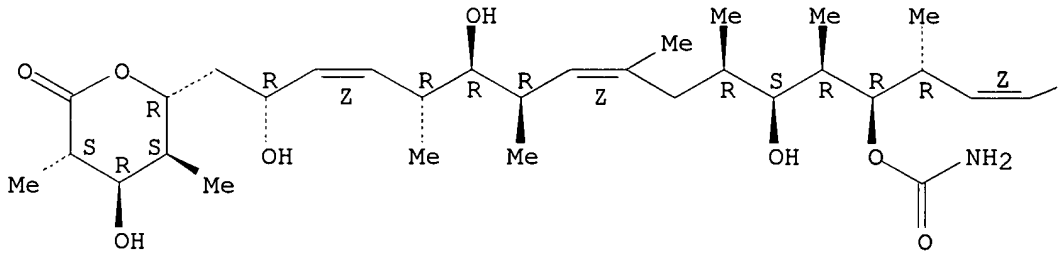
IT **154335-30-5P**, (-)-Discodermolide **194232-29-6P**, 7-epi-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of discodermolide and analogs via a chelation-controlled alkylation)

RN 154335-30-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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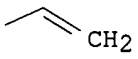
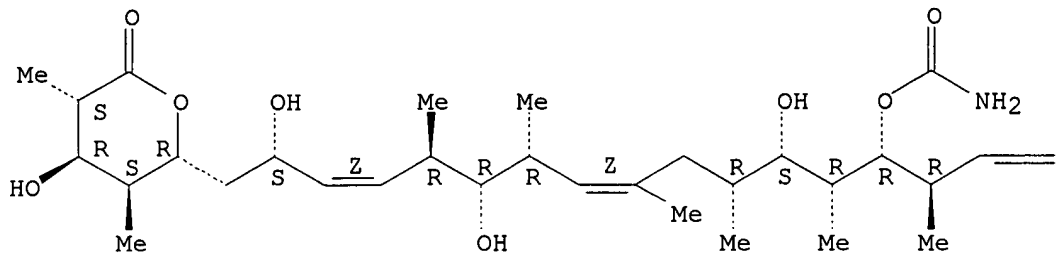


RN 194232-29-6 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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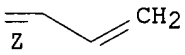


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 72 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:642722 CAPLUS
DOCUMENT NUMBER: 130:38235
TITLE: Total Synthesis of (+)-Discodermolide
AUTHOR(S): Marshall, James A.; Johns, Brian A.
CORPORATE SOURCE: Department of Chemistry, University of Virginia, Charlottesville, VA, 22901, USA
SOURCE: Journal of Organic Chemistry (1998), 63(22), 7885-7892
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:38235
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total synthesis of (+)-discodermolide (I) is described. The approach involves assemblage of three key stereotriad subunits through addn. of nonracemic allenyltin, -indium, and -zinc reagents to (S)-3-silyloxy-2-methylpropanal derivs., followed by redn. of the resulting anti,syn- or syn,syn-homopropargylic alc. adducts to the (E)-homoallylic alcs. and subsequent Sharpless epoxidn. Addn. of Me cuprate reagents or Red-Al to the resultant epoxy alcs. yielded the key precursors, (2S,3S,4S)-HC.tplbond.CCH(.alpha.Me)CH(.beta.OCH2OMe)CH(.beta.Me)CH2OSiEt3 (II), aldehyde (III), and (2S,3R,4S,5S,6Z)-HOCH2CH(.alpha.Me)CH(.alpha.OCH2C6H4-4-OMe)CH(.alpha.Me)CH(.alpha.OSiEt3)CH(.beta.Me)CH=CHCH=CH2 (IV). Addn. of alkyne II (as the lithio species) to aldehyde III afforded the propargylic alc. (V) as the major stereoisomer. Lindlar hydrogenation and installation of appropriate protecting groups led to an aldehyde which was converted to the (Z)-vinylic iodide (VI) upon treatment with

.alpha.-iodoethylidene triphenylphosphorane. Suzuki coupling of this vinylic iodide with a boranate derived from iodide of IV led to the coupled product (VII) with the complete carbon backbone of (+)-discodermolide and the correct stereochem. The synthesis was completed by cleavage of the cyclic PMP acetal at C1 with i-Bu2AlH and three-step oxidn.-esterification to the ester. Cleavage of the C19 Et3Si ether and C19 carbamate formation followed by cleavage of the remaining alc. protecting groups, first with DDQ and then aq. HCl, afforded I.

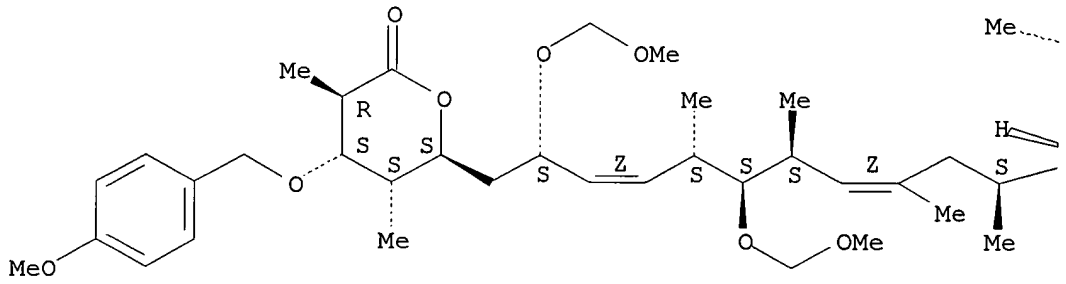
IT **216670-44-9**
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(total synthesis of (+)-discodermolide)

RN 216670-44-9 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2,6-bis(methoxymethoxy)-12-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-[(4-methoxyphenyl)methoxy]-3,5-dimethyl-, (3R,4S,5S,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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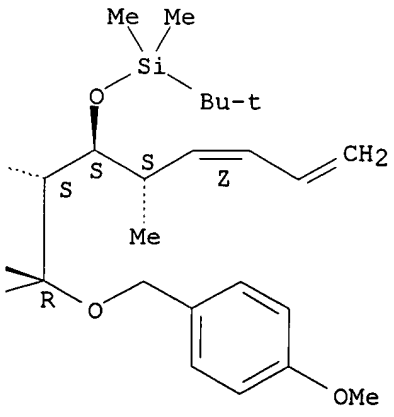


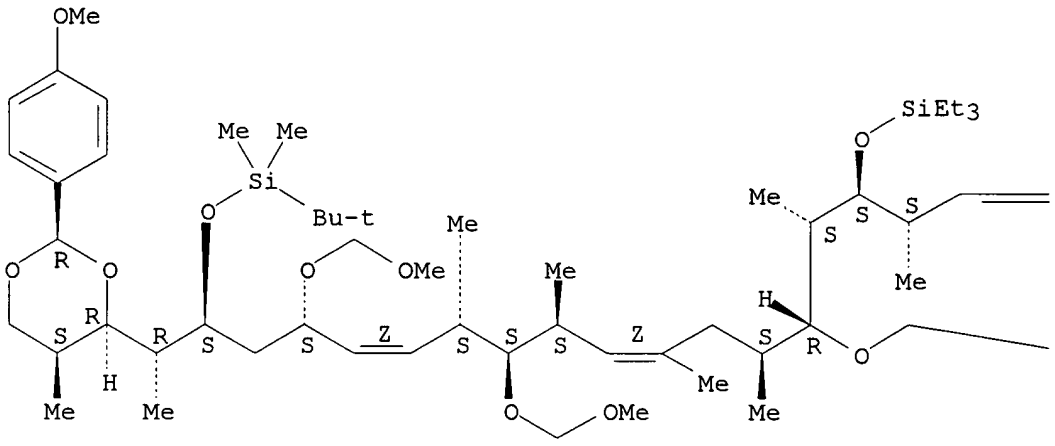
IT **216669-75-9P 216669-84-0P 216669-91-9P**

216669-99-7P 216670-06-3P 216670-11-0P
216670-21-2P 216670-28-9P 216670-34-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of (+)-discodermolide)

RN 216669-75-9 CAPLUS
CN 4,20-Dioxa-3,21-disilatricosa-8,13-diene, 21,21-diethyl-7,11-bis(methoxymethoxy)-17-[(4-methoxyphenyl)methoxy]-5-[(1R)-1-[(2R,4R,5S)-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl]ethyl]-2,2,3,3,10,12,14,16,18-nonamethyl-19-[(1S,2Z)-1-methyl-2,4-pentadienyl]-, (5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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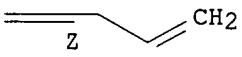
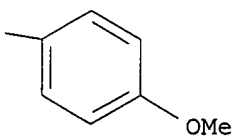


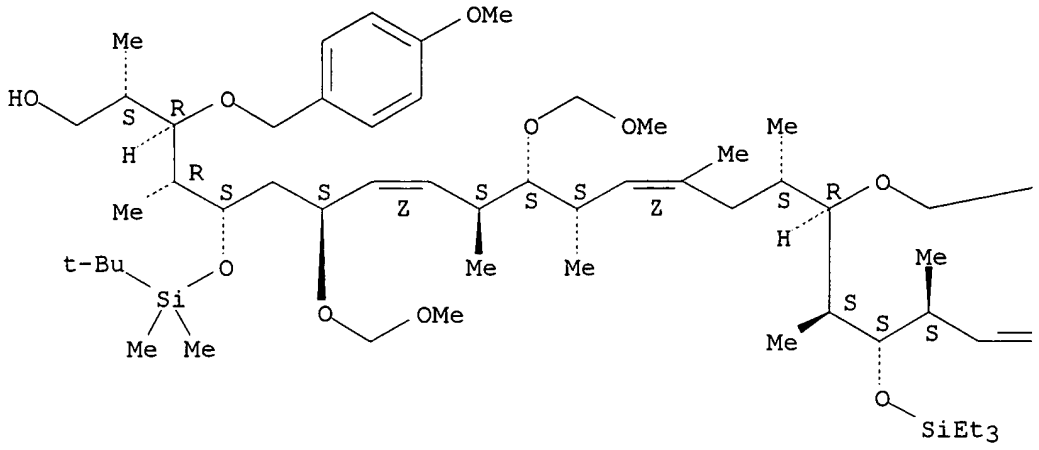


RN 216669-84-0 CAPLUS
CN 8,13,21,23-Tetracosatetraen-1-ol, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-19-[(triethylsilyl)oxy]-, (2S,3R,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA

INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



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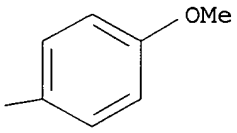
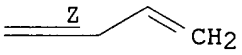
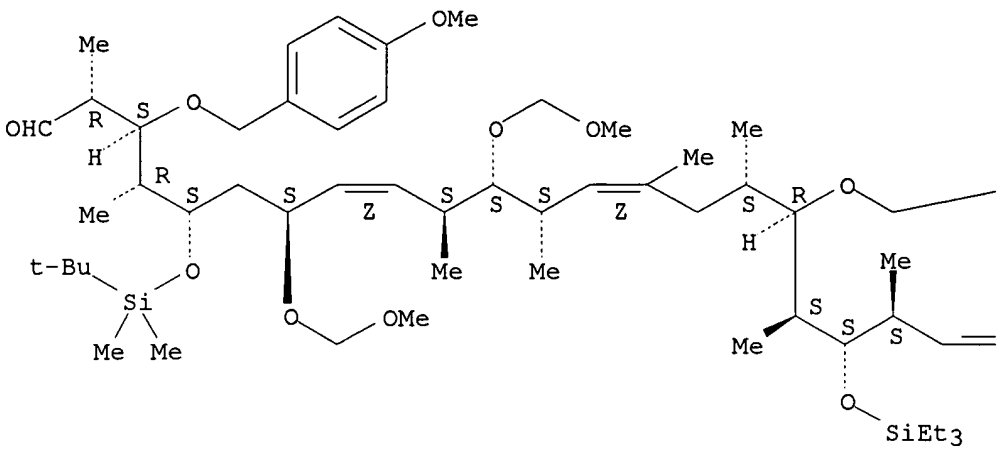




RN 216669-91-9 CAPLUS
CN 8,13,21,23-Tetracosatetraenal, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-19-[(triethylsilyl)oxy]-, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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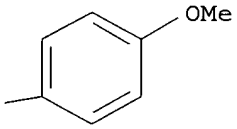
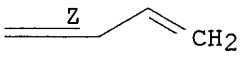
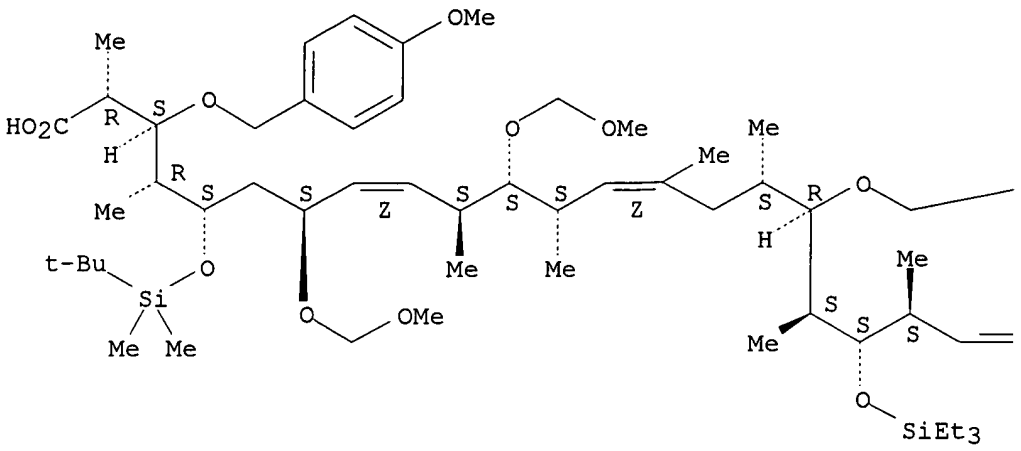




RN 216669-99-7 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-19-[(triethylsilyl)oxy]-, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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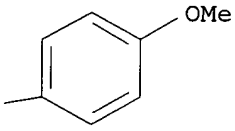
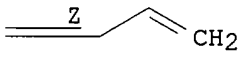
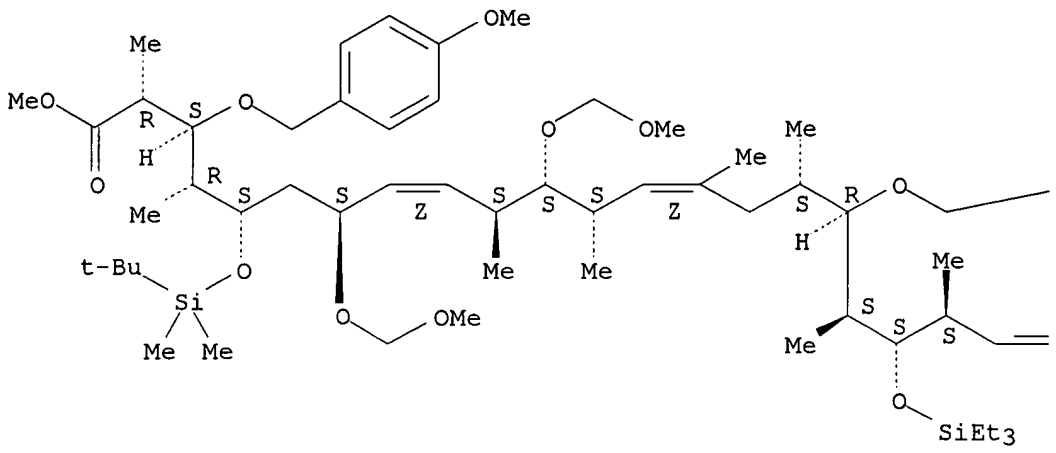




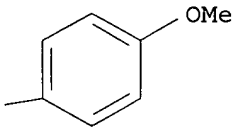
RN 216670-06-3 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-19-[(triethylsilyl)oxy]-, methyl ester, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

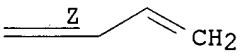
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

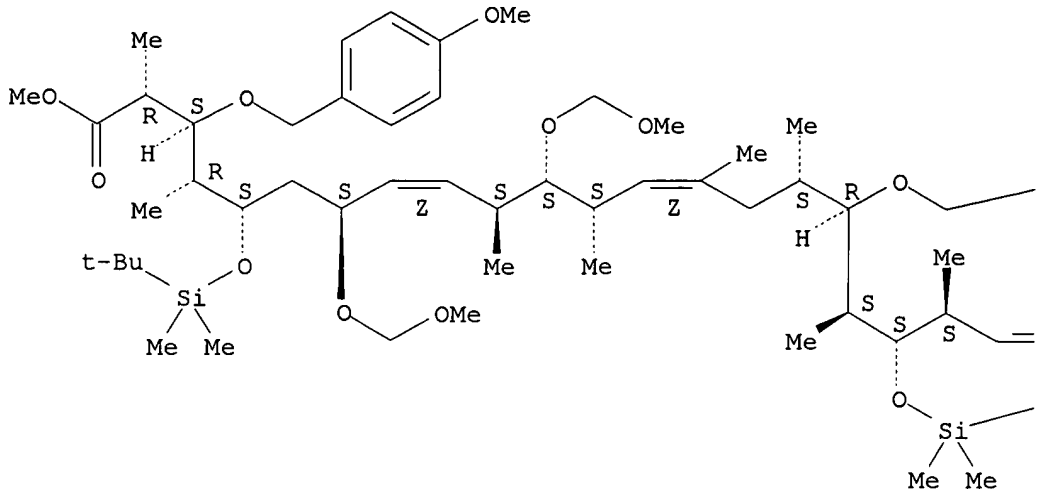




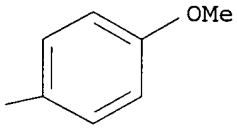
RN 216670-11-0 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 5,19-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

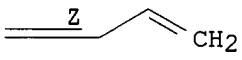
Absolute stereochemistry.
Double bond geometry as shown.

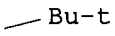
PAGE 1-A



PAGE 1-B



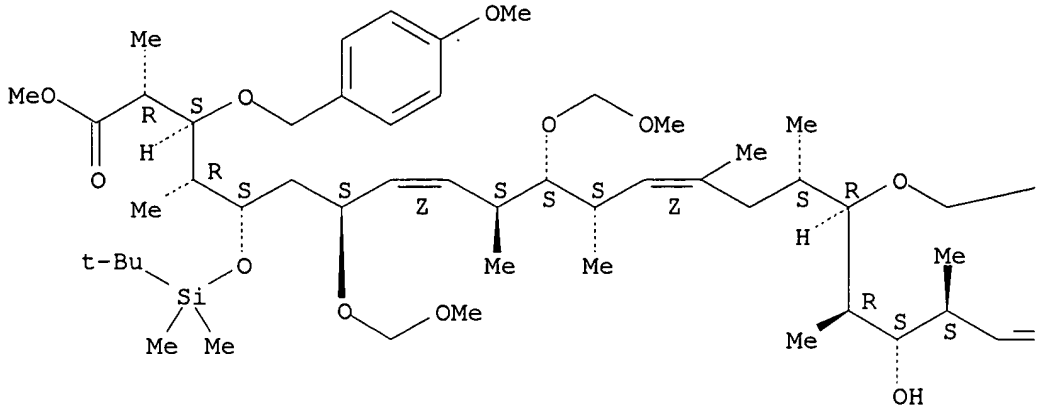




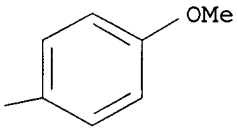
RN 216670-21-2 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-19-hydroxy-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18R,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

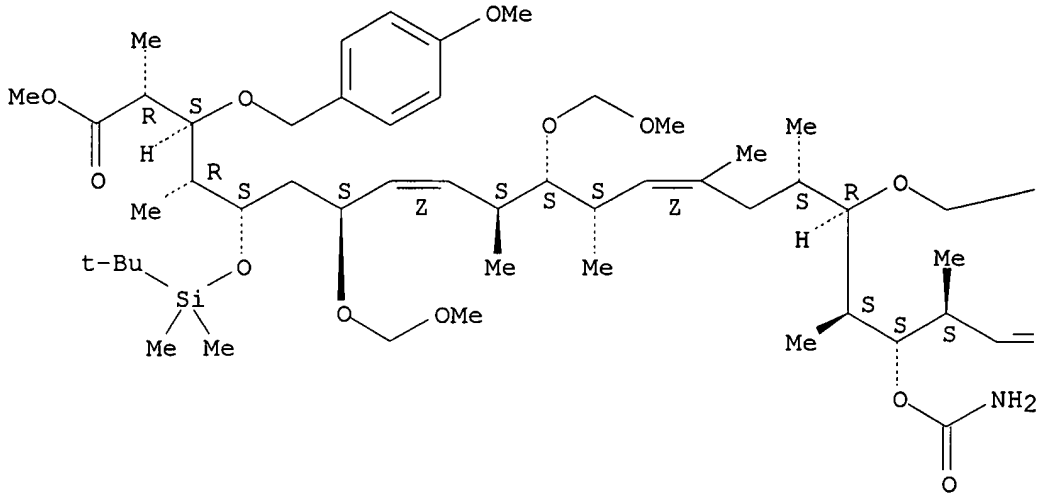


RN 216670-28-9 CAPLUS

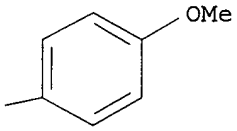
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7,11-bis(methoxymethoxy)-3,17-bis[(4-methoxyphenyl)methoxy]-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



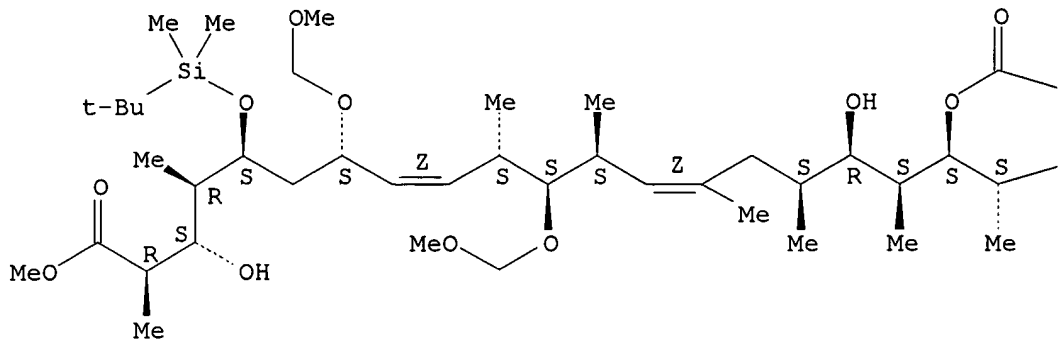
PAGE 1-B



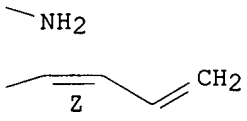
RN 216670-34-7 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-3,17-dihydroxy-7,11-bis(methoxymethoxy)-2,4,10,12,14,16,18,20-octamethyl-, methyl ester, (2R,3S,4R,5S,7S,8Z,10S,11S,12S,13Z,16S,17R,18S,19S,20S,21Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



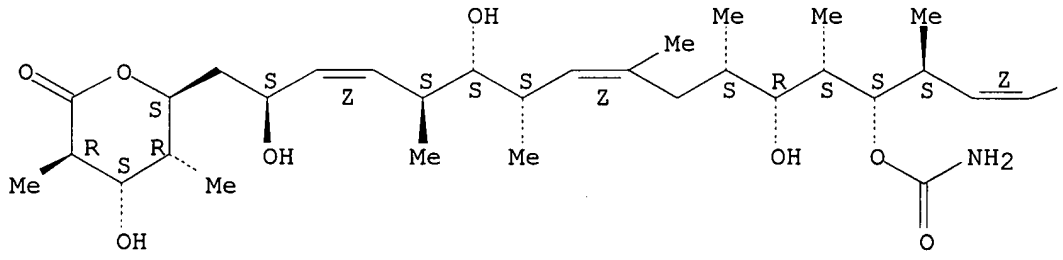
PAGE 1-B



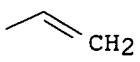
IT **127943-53-7P**, (+)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (+)-discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 73 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:394202 CAPLUS
DOCUMENT NUMBER: 129:67649
TITLE: Synthetic techniques and intermediates for polyhydroxy, dienyllactones and mimics thereof
INVENTOR(S): Smith, Amos B., III; Qiu, Yuping; Kaufman, Michael; Arimoto, Hirokaza; Jones, David R.; Kobayashi, Kaoru
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824429	A1	19980611	WO 1997-US21798	19971201
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5789605	A	19980804	US 1996-759817	19961203
EP 969829	A1	20000112	EP 1997-949661	19971201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515466	T2	20010918	JP 1998-525683	19971201

PRIORITY APPLN. INFO.: US 1996-759817 A 19961203
WO 1997-US21798 W 19971201
OTHER SOURCE(S): CASREACT 129:67649; MARPAT 129:67649
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

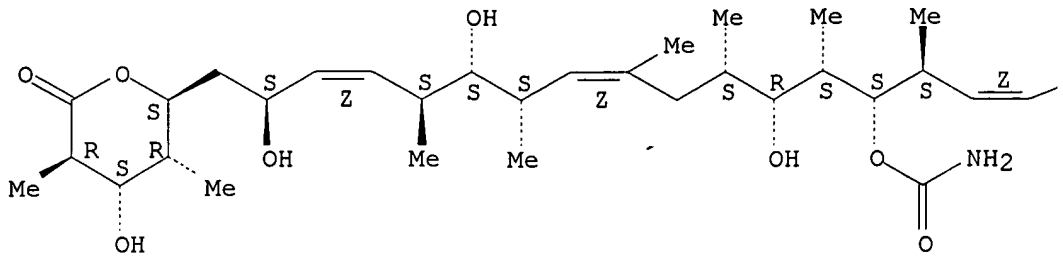
AB Synthesis of discodermolide and intermediates for polyhydroxy, dienyllactones and mimics (I) [R1, R2, R3, R6, R7, R8, R11, R12, R13, R16 = alkyl; Z, Z1, Z2 = O, S, (un)substituted N; R4, R9, R14, R15 = acid labile protecting groups] are described. Thus, reaction of phosphonium salt (II) (R18 = aryl; X = halogen) with base and an alkylthiol (III) [Y = O, S, (un)substituted N] gives diene I. I are useful in the suppression of graft vs. host disease (no data).

IT **127943-53-7P**, Discodermolide
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of discodermolide and intermediates for polyhydroxy, dienyllactones and mimics)

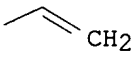
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



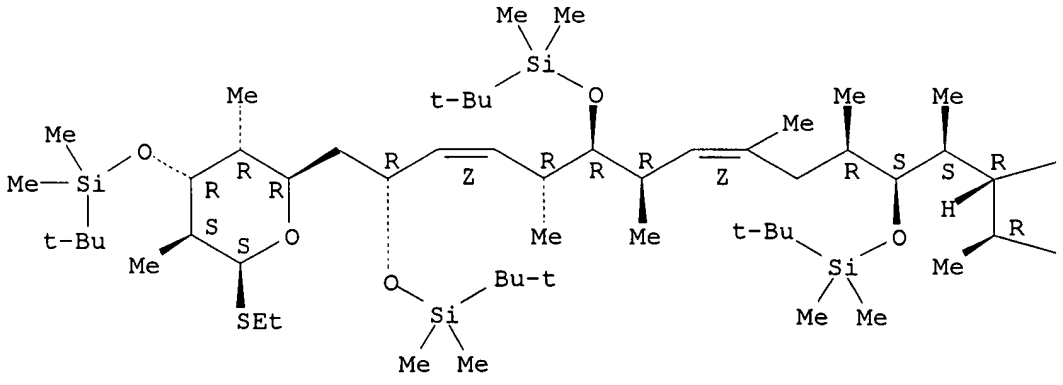
IT **208984-62-7P 208984-63-8P 208984-64-9P**
208984-65-0P 208984-66-1P 208984-67-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of discodermolide and intermediates for polyhydroxy, dienyllactones and mimics)

RN 208984-62-7 CAPLUS

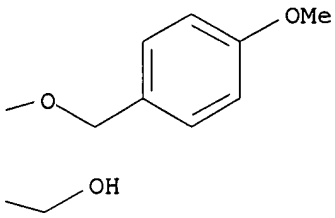
CN 8,13-Hexadecadien-1-ol, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2R,3R,4S,5S,6R,8Z,10R,11R,12R,13Z,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



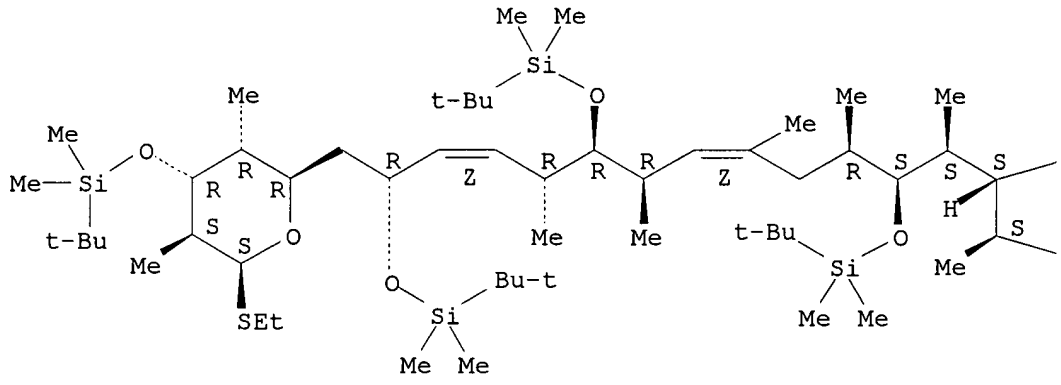
PAGE 1-B



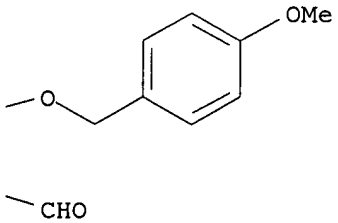
RN 208984-63-8 CAPLUS
CN 8,13-Hexadecadienal, 5,11,15-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-16-[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-pyran-2-yl]-3-[(4-methoxyphenyl)methoxy]-2,4,6,8,10,12-hexamethyl-, (2S,3S,4S,5S,6R,8Z,10R,11R,12R,13Z,15R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

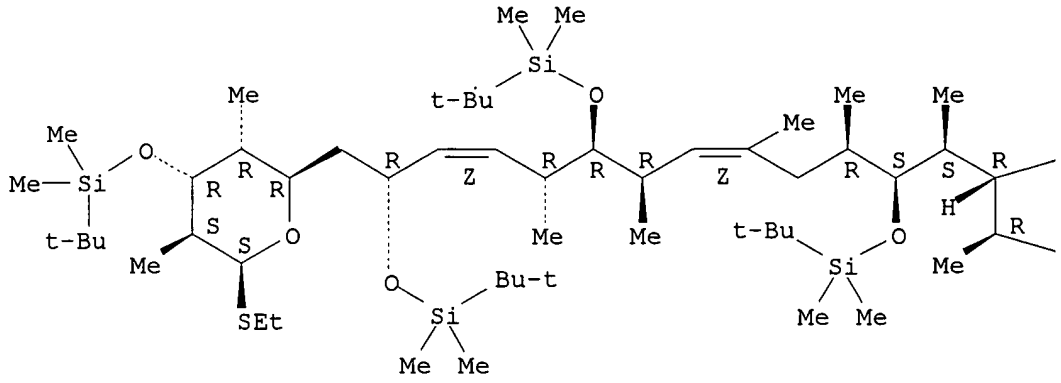


RN 208984-64-9 CAPLUS
CN 4,16-Dioxa-3,17-disilanonadeca-6,11-diene, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[(2R,3R,4R,5S,6S)-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-6-(ethylthio)tetrahydro-3,5-dimethyl-2H-

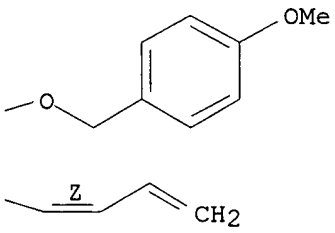
pyran-2-yl]methyl]-15-[(1S,2R,3R,4Z)-2-[(4-methoxyphenyl)methoxy]-1,3-dimethyl-4,6-heptadienyl]-2,2,3,3,8,10,12,14,17,17,18,18-dodecamethyl-, (5R,6Z,8R,9R,10R,11Z,14R,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



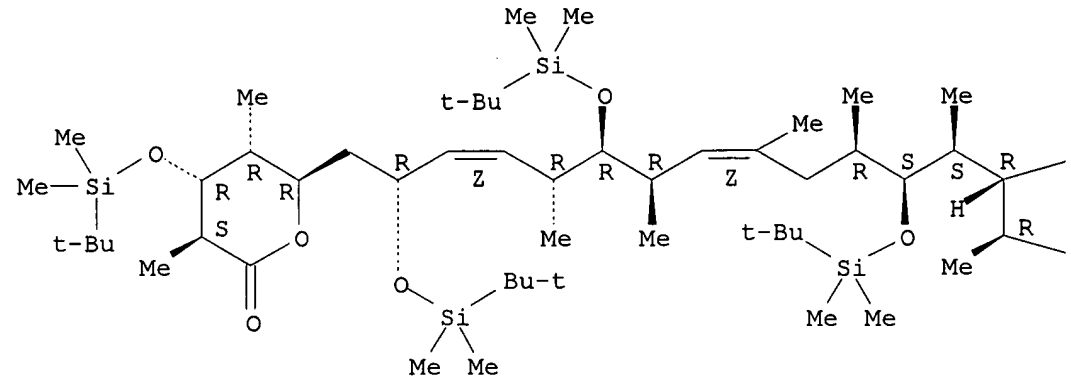
PAGE 1-B



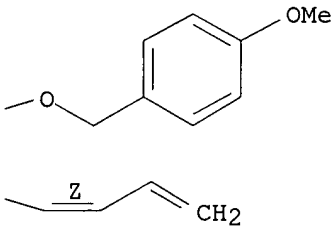
RN 208984-65-0 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13S,14R,15R,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3S,4R,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



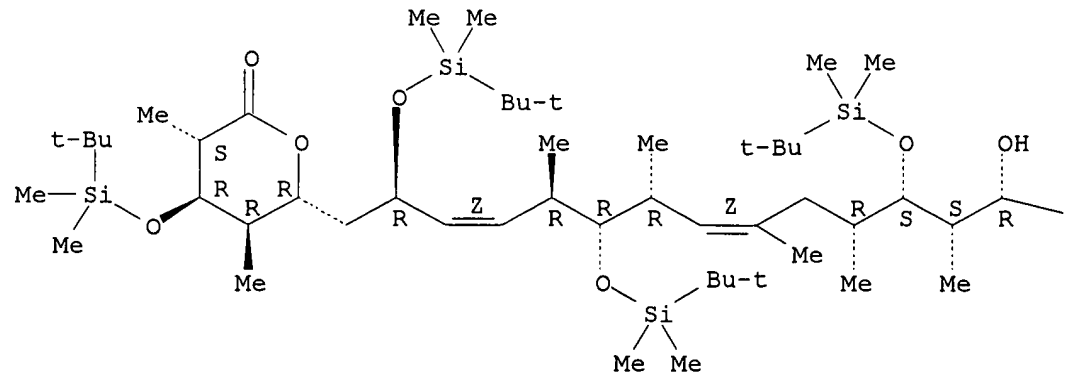
PAGE 1-B



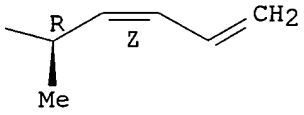
RN 208984-66-1 CAPLUS
CN 2H-Pyran-2-one, 4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13S,14R,15R,16Z)-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, (3S,4R,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



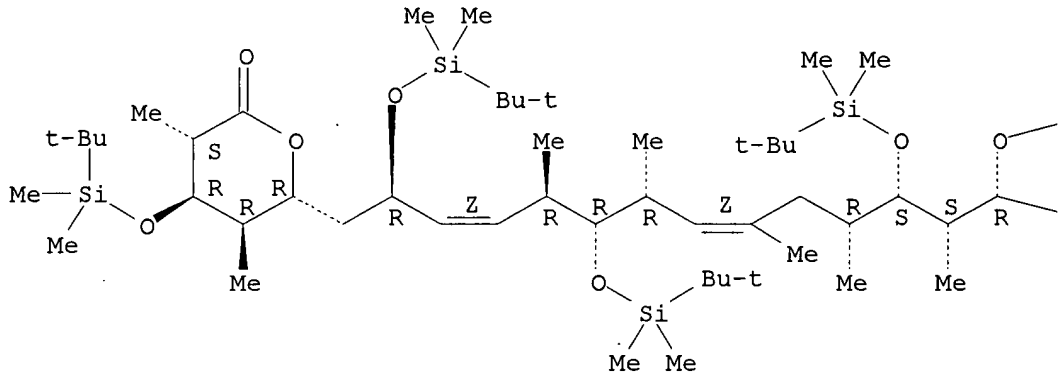
PAGE 1-B



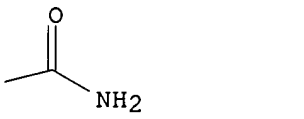
RN 208984-67-2 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13S,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-tris[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, (3S,4R,5R,6R)-(9CI) (CA INDEX NAME)

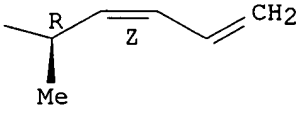
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B





REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 74 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:394200 CAPLUS
DOCUMENT NUMBER: 129:58808
TITLE: Antimicrotubule compositions and methods for treating or preventing inflammatory diseases
INVENTOR(S): Hunter, William L.
PATENT ASSIGNEE(S): Angiotech Pharmaceuticals, Inc., Can.; Hunter, William L.
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824427	A2	19980611	WO 1997-CA910	19971202
WO 9824427	A3	19981001		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 2002037919	A1	20020328	US 1997-980549	19971201
AU 9851132	A1	19980629	AU 1998-51132	19971202
AU 735655	B2	20010712		
EP 941089	A2	19990915	EP 1997-945697	19971202
EP 941089	B1	20010516		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1246791	A	20000308	CN 1997-181581	19971202
BR 9713673	A	20001031	BR 1997-13673	19971202
EP 1070502	A2	20010124	EP 2000-123557	19971202
EP 1070502	A3	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503785	T2	20010321	JP 1998-524997	19971202
JP 3287852	B2	20020604		
EP 1090637	A2	20010411	EP 2000-123537	19971202
EP 1090637	A3	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1092433	A2	20010418	EP 2000-123534	19971202
EP 1092433	A3	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ES 2157601	T3	20010816	ES 1997-945697	19971202
JP 2002226399	A2	20020814	JP 2001-401899	19971202
NO 9902641	A	19990730	NO 1999-2641	19990601
US 2002013298	A1	20020131	US 1999-368463	19990804

PRIORITY APPLN. INFO.:		
US 1996-32215P	P	19961202
US 1997-63087P	P	19971024
US 1997-980549	A2	19971201
EP 1997-945697	A3	19971202
JP 1998-524997	A3	19971202
WO 1997-CA910	W	19971202
US 1998-88546	A3	19980601

AB The present invention provides methods for treating or preventing inflammatory diseases such as psoriasis or multiple sclerosis, comprising the step of delivering to the site of inflammation an anti-microtubule agent, or analog or deriv. thereof. Antimicrotubule agents include epothilone A or B, discodermolide, deuterium oxide, hexylene glycol, tubercidin, LY290181, aluminum fluoride, ethylene glycol bis(succinimidylsuccinate), glycine Et ester, and paclitaxel.

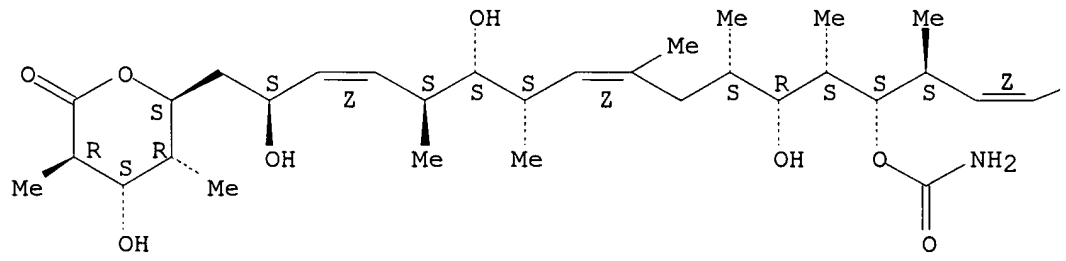
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antimicrotubule compns. and methods for treating or preventing inflammatory diseases)

RN 127943-53-7 CAPLUS

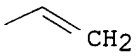
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 75 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:222633 CAPLUS
DOCUMENT NUMBER: 128:308332
TITLE: The total synthesis of (-)-discodermolide
AUTHOR(S): Qiu, Yuping
CORPORATE SOURCE: Univ. of Pennsylvania, Philadelphia, PA, USA
SOURCE: (1997) 350 pp. Avail.: UMI, Order No. DA9814905
From: Diss. Abstr. Int., B 1998, 58(11), 5972
DOCUMENT TYPE: Dissertation
LANGUAGE: English

AB Unavailable

IT **154335-30-5P**, (-)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-discodermolide)

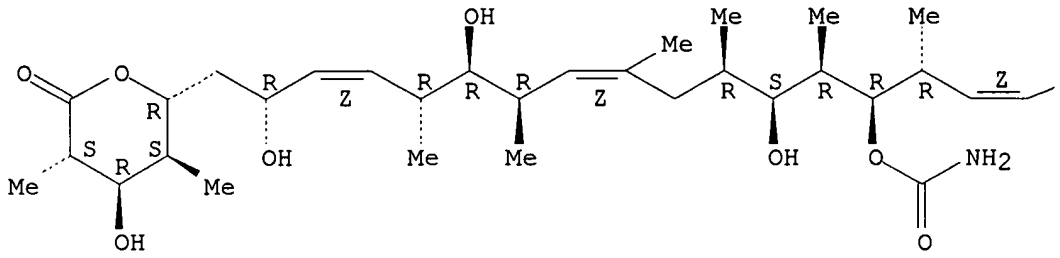
RN 154335-30-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-

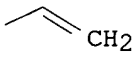
nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 76 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:80882 CAPLUS
DOCUMENT NUMBER: 128:212823
TITLE: The potent microtubule-stabilizing agent (+)-discodermolide induces apoptosis in human breast carcinoma cells-preliminary comparisons to paclitaxel
AUTHOR(S): Balachandran, Raghavan; ten Haar, Ernst; Welsh, Manda J.; Grant, Stepen G.; Day, Billy W.
CORPORATE SOURCE: Department of Environmental & Occupational Health, University of Pittsburgh, Pittsburgh, PA, 15238, USA
SOURCE: Anti-Cancer Drugs (1998), 9(1), 67-76
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Rapid Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (+)-Discodermolide, a sponge-derived natural product, stabilizes microtubules more potently than paclitaxel despite the lack of any obvious structural similarities between the drugs. It competitively inhibits the binding of paclitaxel to tubulin polymers, hypernucleates microtubule assembly more potently than paclitaxel, and inhibits the growth of paclitaxel-resistant ovarian and colon carcinoma cells. Because paclitaxel shows clin. promise for breast cancer treatment, its effects in a series of human breast cancer cells were compared to those of (+)-discodermolide. Growth inhibition, cell and nuclear morphol., and electrophoretic and flow cytometric analyses were performed on (+)-discodermolide-treated MCF-7 and MDA-MB231 cell. (+)-Discodermolide potently inhibited the growth occurred with 10 nM or greater of each drug and was not reversed by removal. (+)-Discodermolide-treated cells exhibited condensed and highly fragmented nuclei. Flow cytometric comparison of cells treated with either drug at 10 nM, a concn. well below that achieved clin. with paclitaxel, showed both caused cell cycle perturbation and induction of a hypodiploid cell population. (+)-Discodermolide caused these effects more extensively and at earlier

time points. The timing and type of high mol. wt. DNA fragmentation induced by the two agents was consistent with induction of apoptosis. The results suggest that (+)-discodermolide has promise as a new chemotherapeutic agent against breast and other cancers.

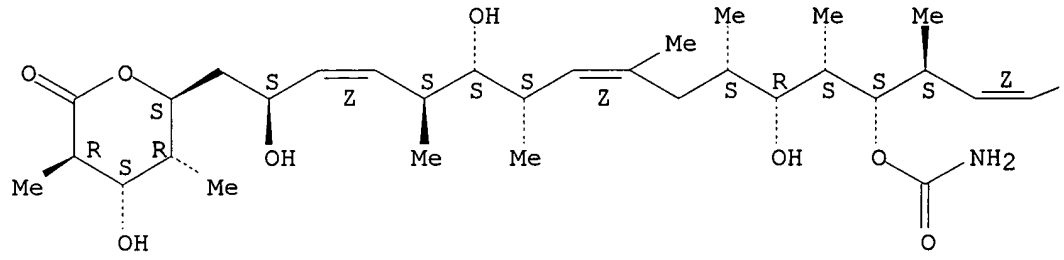
IT **127943-53-7**, (+)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microtubule-stabilizing agent (+)-discodermolide induces apoptosis in human breast carcinoma cells: comparisons to paclitaxel)

RN 127943-53-7 CAPLUS

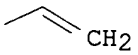
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 77 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:31660 CAPLUS
DOCUMENT NUMBER: 128:34591
TITLE: Total Synthesis of Immunosuppressants: Unified Strategies Exploiting Dithiane Couplings and .sigma.-Bond Olefin Constructions
AUTHOR(S): Smith, Amos B., III; Condon, Stephen M.; McCauley, John A.
CORPORATE SOURCE: Department of Chemistry, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Accounts of Chemical Research (1998), 31(1), 35-46
CODEN: ACHRE4; ISSN: 0001-4842
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 71 refs. in which the total synthesis of (-)-FK506, (-)-rapamycin, (-)-demethoxyrapamycin, and (+)-discodermolide are discussed.

IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)

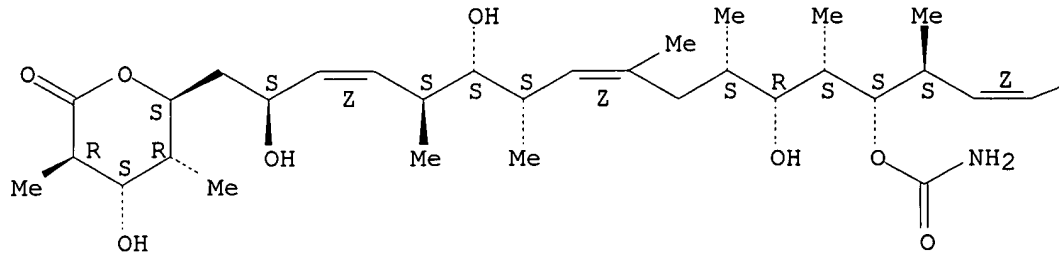
(total synthesis of immunosuppressants, unified strategies exploiting dithiane couplings and .sigma.-bond olefin constructions)

RN 127943-53-7 CAPLUS

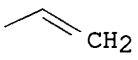
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 78 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:800908 CAPLUS

DOCUMENT NUMBER: 128:75227

TITLE: Synthesis of the C8-C15 segment of (+)-discodermolide

AUTHOR(S): Miyazawa, Masahiro; Oonuma, Satoshi; Maruyama, Kimiyuki; Miyashita, Masaaki

CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060, Japan

SOURCE: Chemistry Letters (1997), (12), 1193-1194
CODEN: CMLTAG; ISSN: 0366-7022

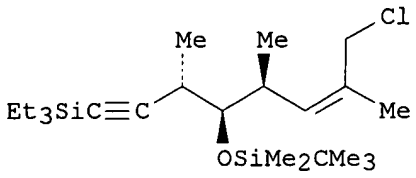
PUBLISHER: Chemical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:75227

GI



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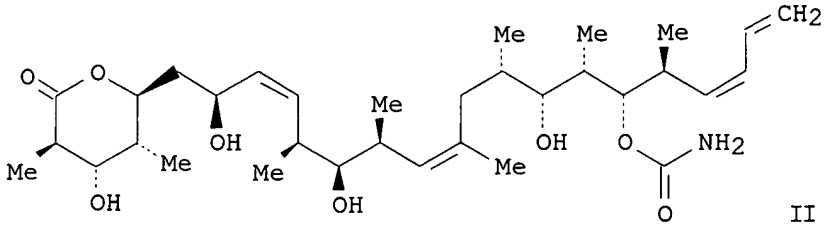


II

AB Succeeding to the preceding paper, stereoselective synthesis of the C8-C15 segment I of (+)-discodermolide (II), the marine natural product having the potent immunosuppressive activity, is described in which the contiguous asym. centers at C11 and C12 positions were stereospecifically constructed via the methylation of an epoxy alc. with lithium dimethylcuprate.

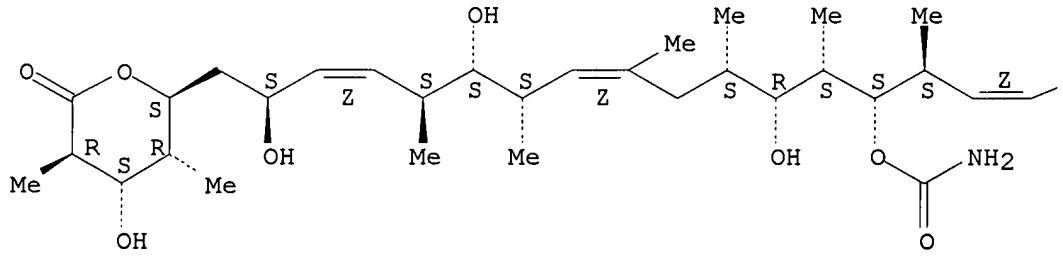
IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(stereoselective synthesis of the C(8)-C(15) segment of (+)-discodermolide)

RN 127943-53-7 CAPLUS

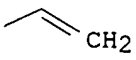
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

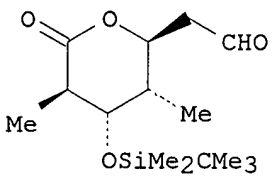
PAGE 1-A



PAGE 1-B



L4 ANSWER 79 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:800907 CAPLUS
DOCUMENT NUMBER: 128:88707
TITLE: Stereoselective synthesis of the C1-C7 segment of (+)-discodermolide
AUTHOR(S): Miyazawa, Masahiro; Oonuma, Satoshi; Maruyama, Kimiyuki; Miyashita, Masaaki
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060, Japan
SOURCE: Chemistry Letters (1997), (12), 1191-1192
CODEN: CMLTAG; ISSN: 0366-7022
PUBLISHER: Chemical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:88707
GI



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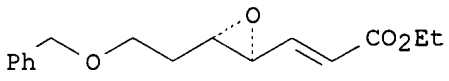
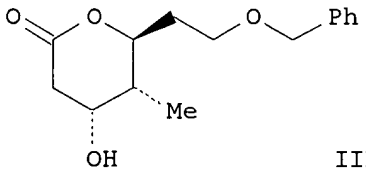
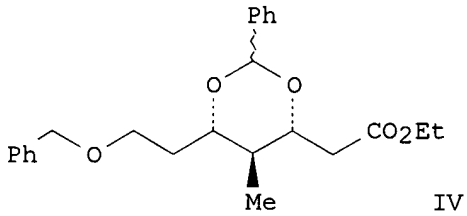


II



III



IV

AB A new and highly stereoselective synthesis of the C1-C7 segment of (+)-discodermolide, the marine natural product having the potent immunosuppressive activity, was described. Aldehyde I, which contains the target C1-C7 segment, was prepd. starting from ester PhCH2O(CH2)2CH:CHCO2Et via stereospecific methylation of .gamma.,.delta.-epoxy acrylate II with Me3Al and formation of lactone III by intramol. conjugate addn. of acetal IV as the key steps.

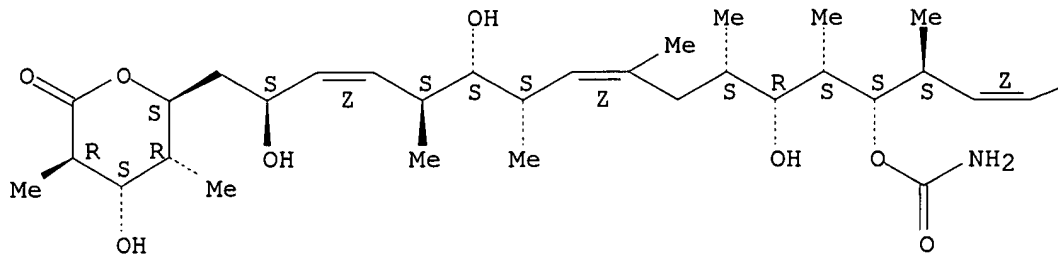
IT **127943-53-7P**, (+)-Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(stereoselective synthesis of the C1-C7 segment of (+)-discodermolide)

RN 127943-53-7 CAPLUS

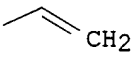
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 80 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:692796 CAPLUS
DOCUMENT NUMBER: 128:10099
TITLE: The microtubule-stabilizing agent discodermolide competitively inhibits the binding of paclitaxel (Taxol) to tubulin polymers, enhances tubulin nucleation reactions more potently than paclitaxel, and inhibits the growth of paclitaxel-resistant cells
AUTHOR(S): Kowalski, Richard J.; Giannakakou, Paraskevi; Gunasekera, Sarath P.; Longley, Ross E.; Day, Billy W.; Hamel, Ernest
CORPORATE SOURCE: Lab. of Drug Discovery Res. and Dev., Dev. Therapeutics Program, Div. of Cancer Treatment, Diagnosis, and Centers, Frederick Cancer Res. and Dev. Cent., Natl. Cancer Inst., Frederick, MD, 21702, USA
SOURCE: Molecular Pharmacology (1997), 52(4), 613-622
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The lactone-bearing polyhydroxylated alkatetraene (+)-discodermolide, which was isolated from the sponge Discodermia dissoluta, induces the polymn. of purified tubulin with and without microtubule-assocd. proteins or GTP, and the polymers formed are stable to cold and calcium. These effects are similar to those of paclitaxel (Taxol), but discodermolide is more potent. The authors confirmed that these properties represent hypernucleation phenomena; the authors obtained lower tubulin crit. concns. and shorter polymers with discodermolide than paclitaxel under a variety of reaction conditions. Furthermore, the authors demonstrated that discodermolide is a competitive inhibitor with [3H]paclitaxel in binding to tubulin polymer, with an apparent Ki value of 0.4 .mu.M. Multidrug-resistant human colon and ovarian carcinoma cells overexpressing P-glycoprotein, which are 900- and 2800-fold resistant to paclitaxel, resp., relative to the parental lines, retained significant sensitivity to discodermolide (25- and 89-fold more resistant relative to the parental lines). Ovarian carcinoma cells that are 20-30-fold more resistant to paclitaxel than the parental line on the basis of expression of altered .beta.-tubulin polypeptides retained nearly complete sensitivity to

discodermolide. The effects of discodermolide on the reorganization of the microtubules of Potorous tridactylis kidney epithelial cells were examd. at different times. Intracellular microtubules were reorganized into bundles in interphase cells much more rapidly after discodermolide treatment compared with paclitaxel treatment. A variety of spindle aberrations were obsd. after treatment with both drugs. The proportions of the different types of aberration were different for the two drugs and changed with the length of drug treatment.

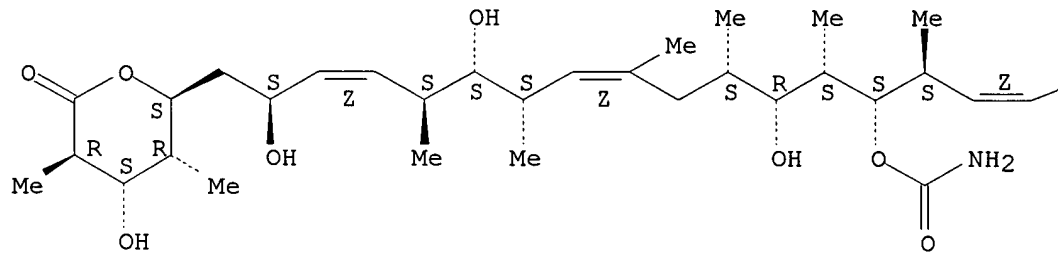
IT **127943-53-7**, (+)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microtubule-stabilizing agent discodermolide competitively inhibits binding of paclitaxel to tubulin polymers and enhances tubulin nucleation reactions more than paclitaxel and inhibits growth of paclitaxel-resistant human tumor cells)

RN 127943-53-7 CAPLUS

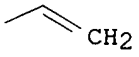
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

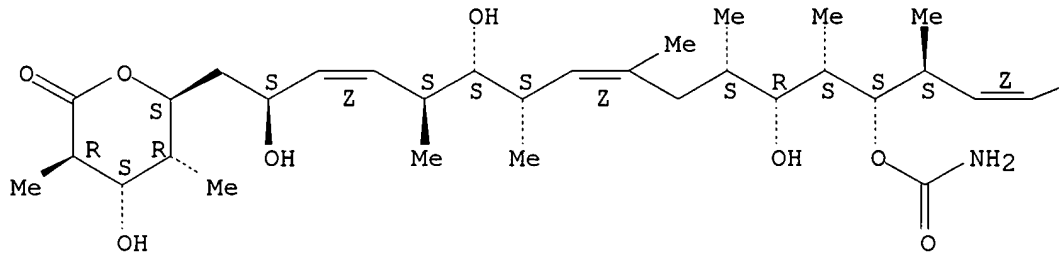


L4 ANSWER 81 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:668564 CAPLUS
DOCUMENT NUMBER: 127:318817
TITLE: Chemical and biological investigations of discodermolide (mitotic arrest, natural products, microtubules)
AUTHOR(S): Hung, Deborah Tan
CORPORATE SOURCE: Harvard Univ., Cambridge, MA, USA
SOURCE: (1996) 303 pp. Avail.: UMI, Order No. DA9733319 From: Diss. Abstr. Int., B 1997, 58(5), 2425
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7P**, Discodermolide

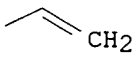
RL: PNU (Preparation, unclassified); PREP (Preparation)
(chem. and biol. investigations of discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 82 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:598135 CAPLUS
DOCUMENT NUMBER: 127:190576
TITLE: Total Synthesis of (-)-Discodermolide: An Application of a Chelation-Controlled Alkylation Reaction
AUTHOR(S): Harried, Scott S.; Yang, Ge; Strawn, Marcus A.; Myles, David C.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, UCLA, Los Angeles, CA, 90095-1569, USA
SOURCE: Journal of Organic Chemistry (1997), 62(18), 6098-6099
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:190576
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The total synthesis of (-)-discodermolide (I) is described. The highly convergent synthetic strategy assemblies discodermolide rapidly from three key precursors. The C-7 to C-8 bond is formed via the Cr(II)/Ni(II)-catalyzed (Nozaki-Kishi) coupling of C-7 aldehyde II to C-8 vinyl iodide III. The C-15 to C-16 bond is formed by a diastereoselective (6:1) chelation-controlled alkylation reaction between C-15 allylic iodide

IV and C-16 enolate anion V.

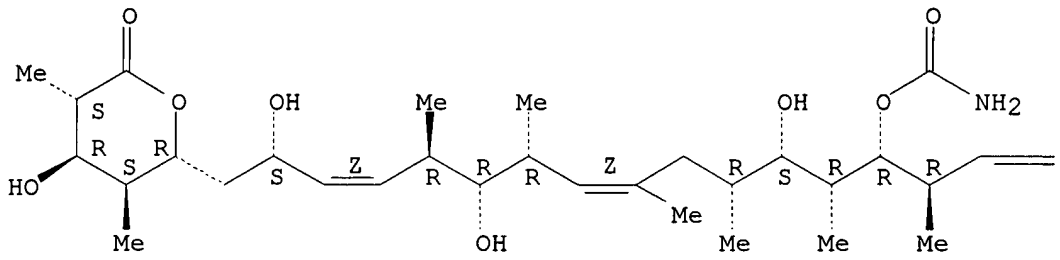
IT **194232-29-6P**, 7-epi-Discodermolide
RL: BYP (Byproduct); PREP (Preparation)
(total synthesis of discodermolide via a chelation-controlled alkylation reaction)

RN 194232-29-6 CAPLUS

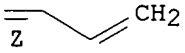
CN 2H-Pyran-2-one, 6-[(2S,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

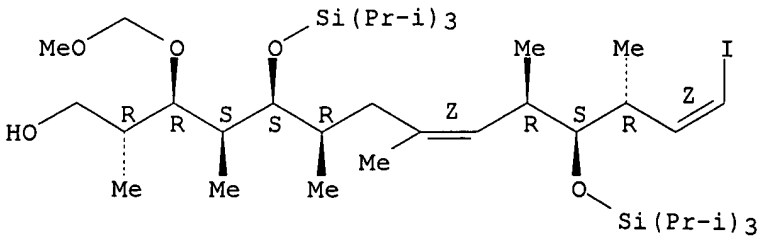


IT **194232-24-1P 194232-25-2P 194232-27-4P**
194232-33-2P 194232-34-3P 194232-35-4P
194232-36-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of discodermolide via a chelation-controlled alkylation reaction)

RN 194232-24-1 CAPLUS

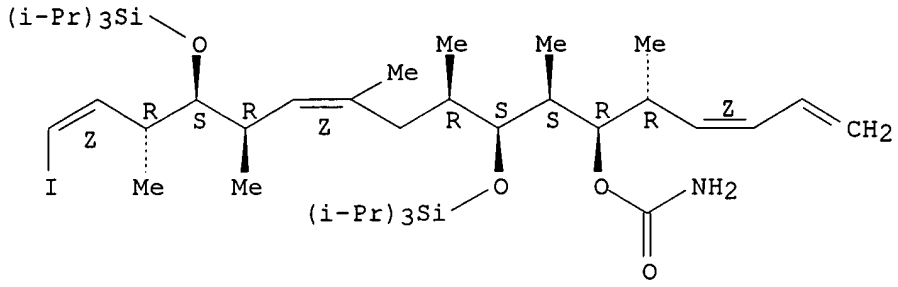
CN 8,13-Tetradecadien-1-ol, 14-iodo-3-(methoxymethoxy)-2,4,6,8,10,12-hexamethyl-5,11-bis[[tris(1-methylethyl)silyl]oxy]-, (2R,3R,4S,5S,6R,8Z,10R,11S,12R,13Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 194232-25-2 CAPLUS
CN 1,3,11,16-Heptadecatetraen-6-ol, 17-iodo-5,7,9,11,13,15-hexamethyl-8,14-bis[[tris(1-methylethyl)silyl]oxy]-, carbamate, (3Z,5R,6R,7S,8S,9R,11Z,13R,14S,15R,16Z)- (9CI) (CA INDEX NAME)

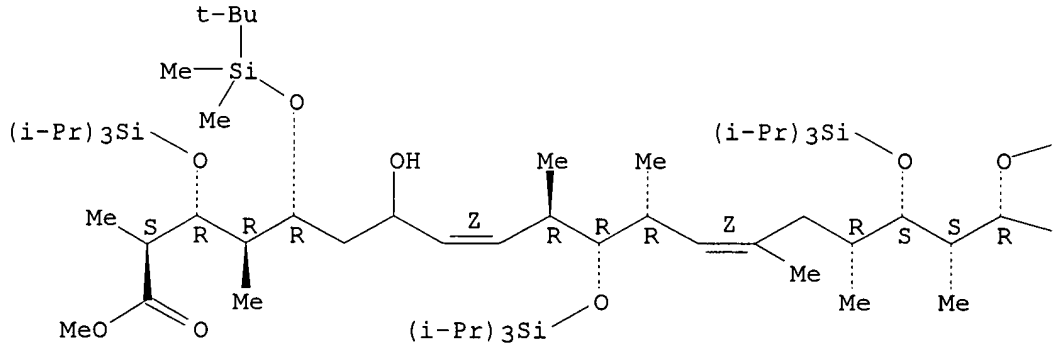
Absolute stereochemistry.
Double bond geometry as shown.

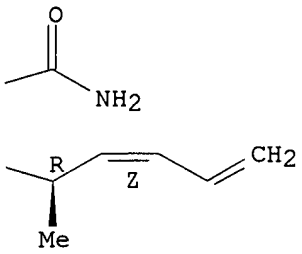


RN 194232-27-4 CAPLUS
CN 8,13,21,23-Tetracosatetraenoic acid, 19-[(aminocarbonyl)oxy]-5-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-7-hydroxy-2,4,10,12,14,16,18,20-octamethyl-3,11,17-tris[[tris(1-methylethyl)silyl]oxy]-, methyl ester, (2S,3R,4R,5R,8Z,10R,11R,12R,13Z,16R,17S,18S,19R,20R,21Z)-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

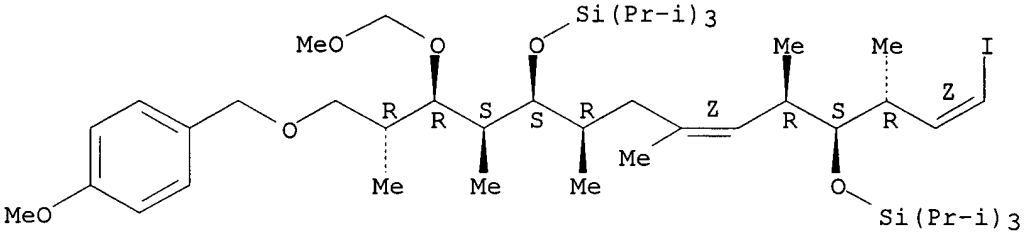
PAGE 1-A





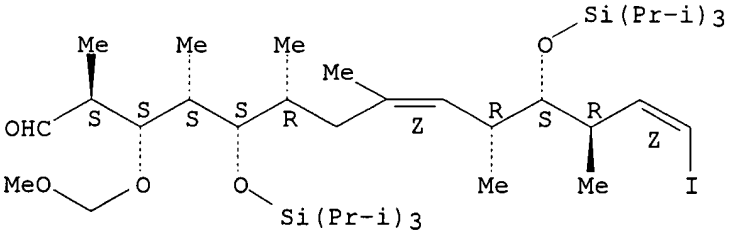
RN 194232-33-2 CAPLUS
CN 2,4,14-Trioxa-15-silaheptadec-10-ene, 13-[(1R,2Z)-3-iodo-1-methyl-2-propenyl]-5-[(1R)-2-[(4-methoxyphenyl)methoxy]-1-methylethyl]-6,8,10,12,16-pentamethyl-15,15-bis(1-methylethyl)-7-[[tris(1-methylethyl)silyl]oxy]-, (5R,6S,7S,8R,10Z,12R,13S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



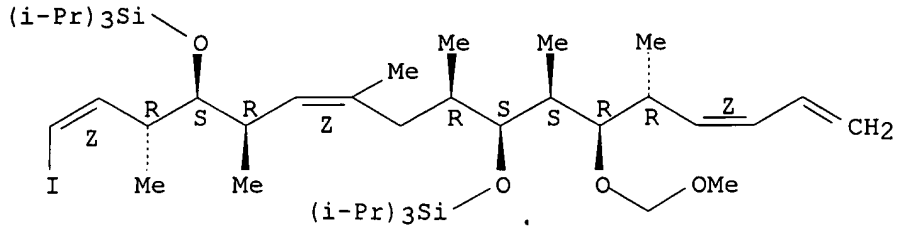
RN 194232-34-3 CAPLUS
CN 8,13-Tetradecadienal, 14-iodo-3-(methoxymethoxy)-2,4,6,8,10,12-hexamethyl-5,11-bis[[tris(1-methylethyl)silyl]oxy]-, (2S,3S,4S,5S,6R,8Z,10R,11S,12R,13Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



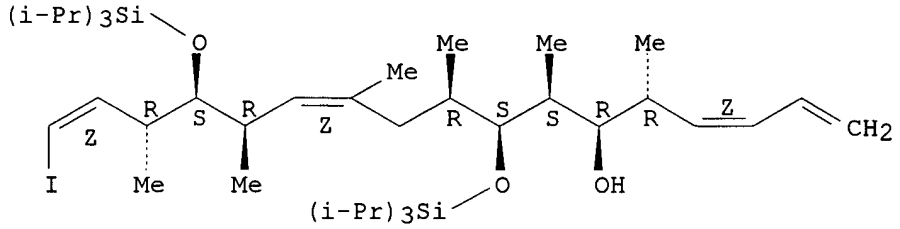
RN 194232-35-4 CAPLUS
CN 2,4,14-Trioxa-15-silaheptadec-10-ene, 13-[(1R,2Z)-3-iodo-1-methyl-2-propenyl]-6,8,10,12,16-pentamethyl-15,15-bis(1-methylethyl)-5-[(1R,2Z)-1-methyl-2,4-pentadienyl]-7-[[tris(1-methylethyl)silyl]oxy]-, (5R,6S,7S,8R,10Z,12R,13S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 194232-36-5 CAPLUS
CN 1,3,11,16-Heptadecatetraen-6-ol, 17-iodo-5,7,9,11,13,15-hexamethyl-8,14-bis[[tris(1-methylethyl)silyl]oxy]-, (3Z,5R,6R,7S,8S,9R,11Z,13R,14S,15R,16Z)- (9CI) (CA INDEX NAME)

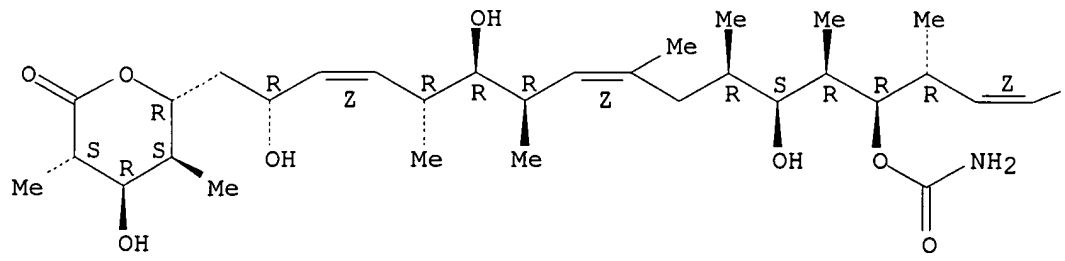
Absolute stereochemistry.
Double bond geometry as shown.



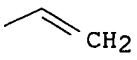
IT **154335-30-5P**, (-)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of discodermolide via a chelation-controlled alkylation reaction)
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



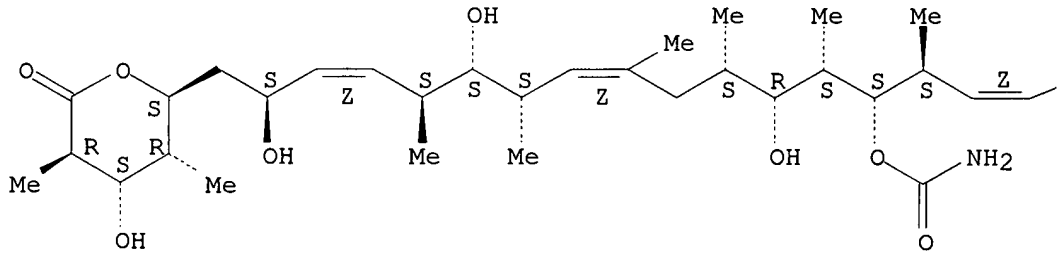
PAGE 1-B



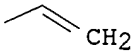
L4 ANSWER 83 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:512360 CAPLUS
DOCUMENT NUMBER: 127:190560
TITLE: Synthetic studies towards discodermolide and a total synthesis of didehydrodiscodermolide
AUTHOR(S): Clark, David Louis
CORPORATE SOURCE: Univ. of California, Berkeley, CA, USA
SOURCE: (1996) 157 pp. Avail.: UMI, Order No. DA9722914
From: Diss. Abstr. Int., B 1997, 58(2), 700
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthetic studies towards discodermolide and total synthesis of didehydrodiscodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 84 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:479358 CAPLUS
DOCUMENT NUMBER: 127:104331
TITLE: Discodermolide compounds and pharmaceutical compositions containing them for cancer therapy
INVENTOR(S): Longley, Ross E.; Gunasekera, Sarath P.; Pomponi, Shirley
PATENT ASSIGNEE(S): Harbor Branch Oceanographic Institution, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9720835	A1	19970612	WO 1996-US19344	19961205
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5681847	A	19971028	US 1995-567442	19951205
CA 2233716	AA	19970612	CA 1996-2233716	19961205
EP 873332	A1	19981028	EP 1996-943591	19961205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000501710	T2	20000215	JP 1997-521410	19961205
JP 3293833	B2	20020617		

PRIORITY APPLN. INFO.: US 1995-567442 A 19951205
WO 1996-US19344 W 19961205

OTHER SOURCE(S): MARPAT 127:104331

AB Discodermolide lactone compds. (from the marine sponge Discodermia dissoluta) and their analogs have been shown to have activity against mammalian cancer cells, and can be used in treating human patients which host cancer cells including leukemia, melanoma, and breast, colon, CNS, and lung tumors. Synthetic prepn. of octahydrodiscodermolide epimers is included, as are the antiproliferative effects of discodermolide on human tumor cell lines and effects of discodermolide on tubulin polymn. and stabilization.

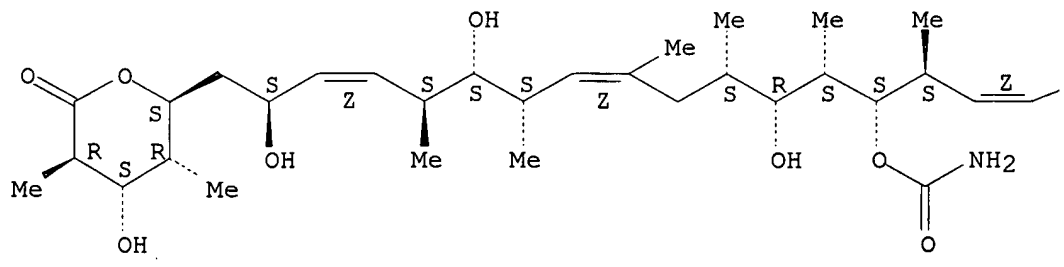
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(discodermolide compds. from Discodermia, and pharmaceutical compns. contg. them for cancer therapy)

RN 127943-53-7 CAPLUS

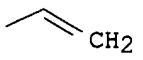
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

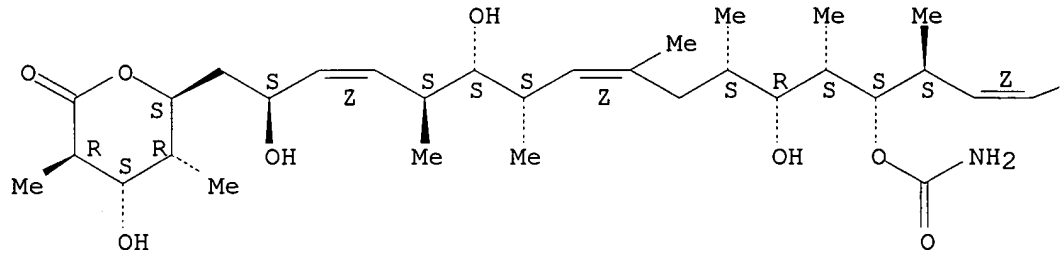


IT **127943-53-7D**, Discodermolide, derivs. **192187-47-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discodermolide compds. from Discodermia, and pharmaceutical compns. contg. them for cancer therapy)

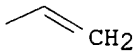
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

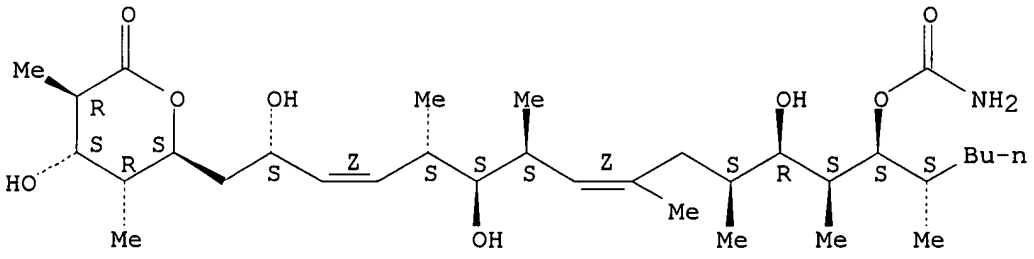


PAGE 1-B



RN 192187-47-6 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8-nonadecadienyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L4 ANSWER 85 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:474298 CAPLUS
DOCUMENT NUMBER: 127:176291

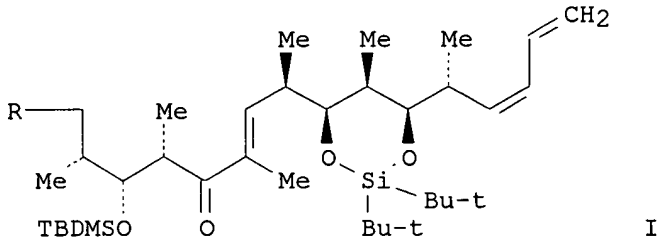
09/730,929

TITLE: Studies towards the total synthesis of the marine-derived immunosuppressant discodermolide: stereoselective synthesis of a C9-C24 subunit

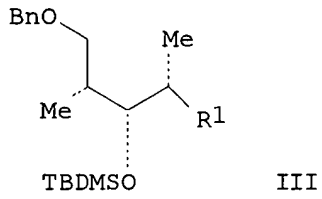
AUTHOR(S): Paterson, Ian; Schlapbach, Achim
CORPORATE SOURCE: Univ. Chemical Lab., Cambridge, CB2 1EW, UK

SOURCE: Synlett (1995), (Spec. Issue), 498-500
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Thieme
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:176291

GI



I



III

AB Enone (I) (R = OCH2Ph) (II), an advanced C9-C24 subunit of discodermolide, was synthesized in 17 steps starting from the Et ketone (R)-PhCH2OCH2CH(Me)COEt. The sequence (III) [R1 = (E)-COC(Me)=CHEt] .fwdarw. III [R1 = (Z)-CH=C(Me)Pr] was developed to introduce the Z-alkene at C13, enabling the conversion of II into the complete segment II (R = =PPh3).

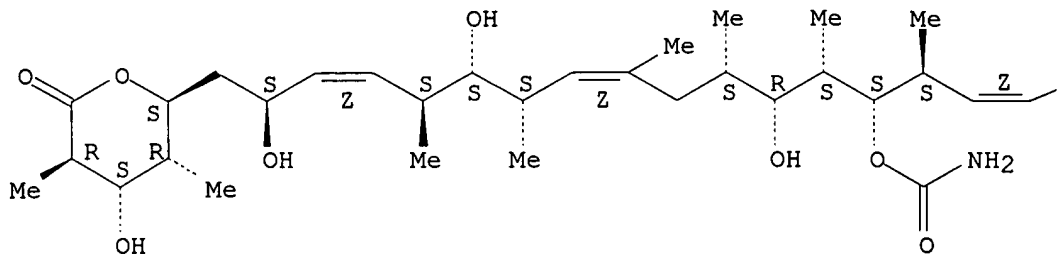
IT **127943-53-7DP**, Discodermolide, C9-C24 subunit
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective synthesis of a C9-C24 subunit discodermolide)

RN 127943-53-7 CAPLUS

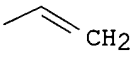
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 86 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:455072 CAPLUS
DOCUMENT NUMBER: 127:156078
TITLE: Epothilones: novel microtubule-stabilizing agents
AUTHOR(S): Bollag, Daniel M.
CORPORATE SOURCE: Merck Res. Lab., West Point, PA, 19486, USA
SOURCE: Expert Opinion on Investigational Drugs (1997), 6(7), 867-873
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 44 refs. The past few years have witnessed the regulatory approvals of the anticancer microtubule stabilizing taxane drugs, Taxol and Taxotere which are rapidly gaining acceptance as important antineoplastic agents with potential against numerous solid tumor malignancies. Despite a basic understanding of the biochem. target of taxanes dating back nearly 20 yr, new classes of tubulin-binding microtubule polymn. enhancers were only reported in the last two years. Epothilones and discodermolide are newly discovered compds., which are structurally distinct from the taxanes, but which possess similar tubulin polymg. and cell biol. effects. In the first studies reported, these compds. displayed similar or greater potencies than taxanes, and the epothilones may represent an advance over the taxanes in retaining toxicity against various taxane-resistant cell lines. This review summarizes the data published on epothilones and discodermolide and proposes further steps that could establish these new classes of compds. as potential second generation microtubule polymn. enhancers.

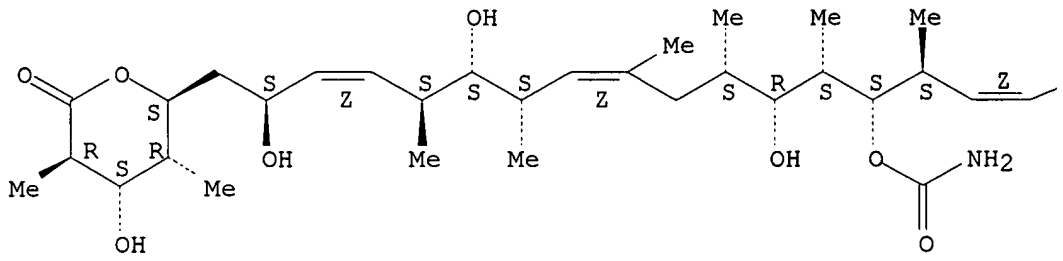
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epothilones and discodermolide as novel microtubule-stabilizing agents in relation to anticancer activity in humans and lab. animals)

RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI)

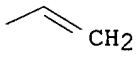
(CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



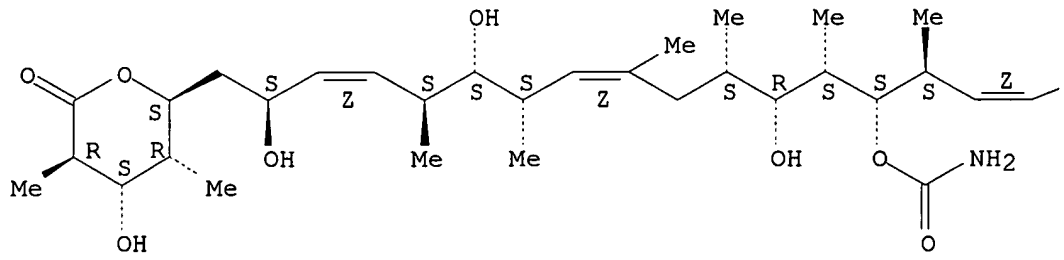
PAGE 1-B



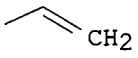
L4 ANSWER 87 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:703757 CAPLUS
DOCUMENT NUMBER: 126:7900
TITLE: Stereospecific alkylation of .gamma.,.delta.-epoxy acrylates by trimethylaluminum and its application to natural product synthesis
AUTHOR(S): Miyazawa, Masahiro; Oonuma, Satoshi; Ueda, Masato; Ishibashi, Naoki; Maruyama, Kimiyuki; Miyashita, Masaaki
CORPORATE SOURCE: Graduate School Science, Hokkaido University, Japan
SOURCE: Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1996), 38th, 661-666
CODEN: TYKYDS
PUBLISHER: Nippon Kagakkai
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lecture on the stereospecific alkylation of .gamma.,.delta.-epoxy acrylates by trimethylaluminum and its application to natural product synthesis.
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(stereospecific methylation of .gamma.,.delta.-epoxy acrylates by trimethylaluminum as a route in natural product synthesis)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 88 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:701793 CAPLUS
DOCUMENT NUMBER: 126:69728
TITLE: Computational and molecular modeling evaluation of the structural basis for tubulin polymerization inhibition by colchicine site agents
AUTHOR(S): ter Haar, Ernst; Rosenkranz, Herbert S.; Hamel, Ernest; Day, Billy W.
CORPORATE SOURCE: Dep. Environmental and Occupational Health, Univ. Pittsburgh Cancer Inst., Pittsburgh, PA, 15238, USA
SOURCE: Bioorganic & Medicinal Chemistry (1996), 4(10), 1659-1671
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The computer-automated structure evaluation programs MultiCASE and CASE were used to perform a quant. structure-activity relationship study on tubulin polymn. inhibitors. A learning set of 536 chems. (202 active, 27 marginal, and 307 inactive), built using IC50 values for inhibition of tubulin polymn. or mitosis from this and previous studies, was used for artificial intelligence self-teaching. The algorithms successfully predicted the activity of agents in the learning set with >90% accuracy. Seventeen MultiCASE and 12 CASE (mostly included in the MultiCASE set) biophores (substructures significantly correlated with activity) were identified with a probability >0.95. Here the authors present the biophores of podophyllotoxins, colchicinoids, and certain combretastatins, each examd. for structure-activity relationships. For the podophyllotoxins and colchicinoids in the learning set, the correlations between obsd. and predicted potencies were >0.85. The algorithms recognized the importance of several known site, electronic, and steric effects in the 2 classes. A predictive QSAR (R2 = 0.98) was developed for combretastatin A-2 and dihydrocombretastatin analogs. The MultiCASE/CASE analyses were used in combination with mol. models to study relative orientations of colchicine, podophyllotoxin, combretastatin A-4, and steganacin at the colchicine site. This resulted in a new hypothesis, consistent with extensive published exptl. data, in which the C-ring and part of the B-ring of colchicine overlap with the A- and B-rings of

podophyllotoxin. Consequently, the trimethoxyphenyl rings of colchicine and podophyllotoxin occupied different regions of space, each pointing out from a hydrophobic core occupied by the overlapping biophores. The mol. model of the highly potent combretastatin A-4 could fit into the model binding site in .gtoreq.3 different ways. The developed QSARs were used to identify the potent microtubule stabilizer discodermolide. Its identification, in concert with recently reported findings, suggest potential overlap in the colchicine and paclitaxel binding sites on tubulin.

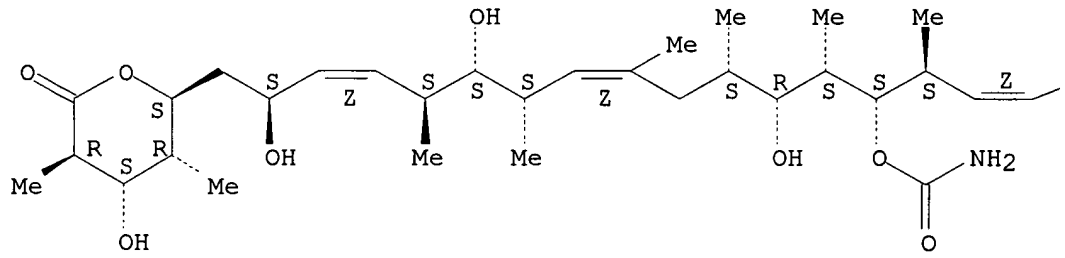
IT **127943-53-7**, Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(computational and mol. modeling evaluation of structural basis for tubulin polymn. inhibition by colchicine site agents)

RN 127943-53-7 CAPLUS

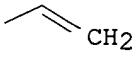
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



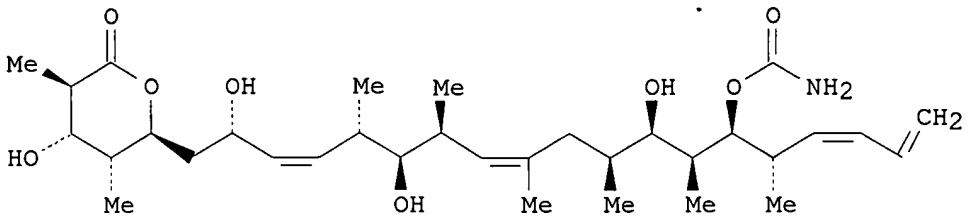
PAGE 1-B



L4 ANSWER 89 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1996:657111 CAPLUS
DOCUMENT NUMBER:	126:31209
TITLE:	Syntheses of Discodermolides Useful for Investigating Microtubule Binding and Stabilization
AUTHOR(S):	Hung, Deborah T.; Nerenberg, Jennie B.; Schreiber, Stuart L.
CORPORATE SOURCE:	Howard Hughes Medical Institute, Harvard University, Cambridge, MA, 02138, USA
SOURCE:	Journal of the American Chemical Society (1996), 118(45), 11054-11080 CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

GI



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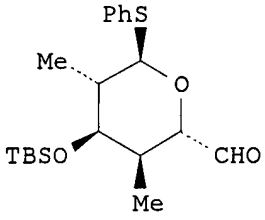

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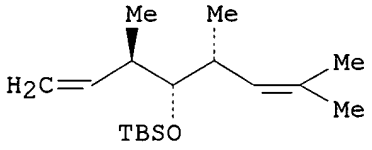
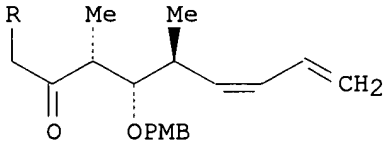


III



IV

AB Discodermolide (I) is a marine natural product reported to inhibit the proliferation of T cells and exhibit immunosuppressive activity. Total syntheses of the natural antipode of discodermolide and several variants are reported. These studies provide reagents to investigate discodermolide's recently discovered ability to bind and stabilize microtubules in cells. Retrosynthetically, the polypropionate is divided into fragments II, III, and IV (R = H, Me) of approx. equal complexity. This modular strategy provides convergency in the synthesis and facilitates the prepn. of discodermolide-based reagents.

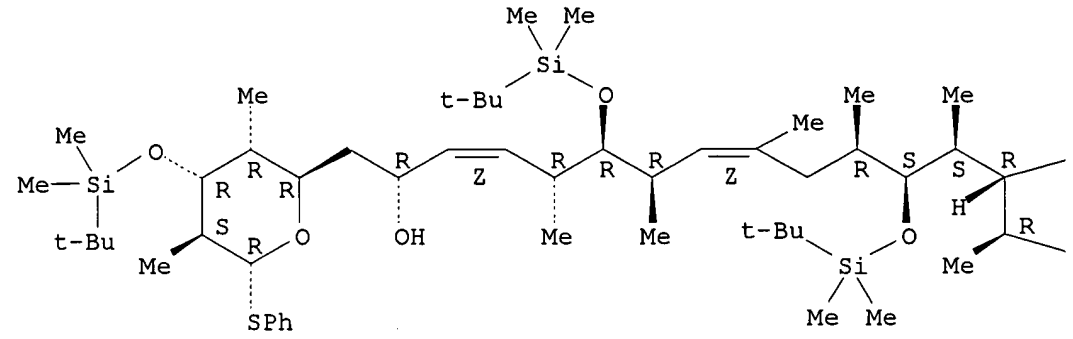
IT **184291-40-5P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(attempted synthesis of discodermolide useful for investigating microtubule binding and stabilization)

RN 184291-40-5 CAPLUS

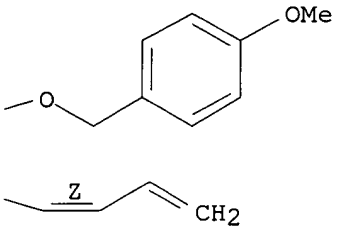
CN 2H-Pyran-2-ethanol, .alpha.-[4,10-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-12-[(4-methoxyphenyl)methoxy]-3,5,7,9,11,13-hexamethyl-1,6,14,16-heptadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-, [2R-[2.alpha.[R*(1Z,3R*,4R*,5R*,6Z,9R*,10S*,11S*,12R*,13R*,14Z)],3.beta.,4.beta.,5.alpha.,6.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



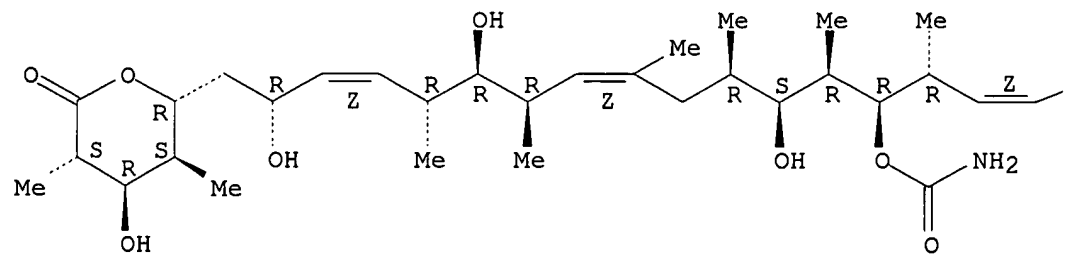
IT **154335-30-5P 184291-46-1P 184291-62-1P**
184291-68-7P 184291-80-3P 184291-81-4P
184291-82-5P 184291-90-5P 184488-81-1P
184488-83-3P 184777-96-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(syntheses of discodermolides useful for investigating microtubule binding and stabilization)

RN 154335-30-5 CAPLUS

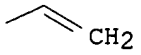
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



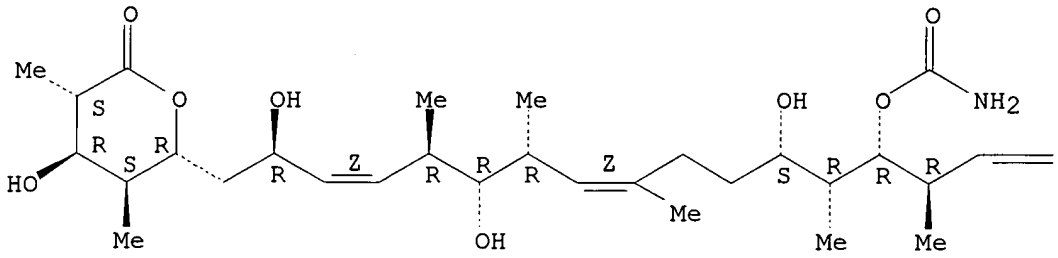
PAGE 1-B



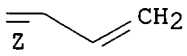
RN 184291-46-1 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,13,15-pentamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,12R*,13R*,14S*,15S*,16Z)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



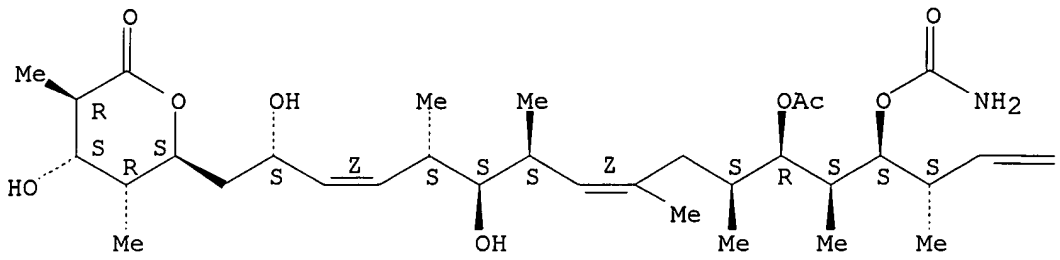
PAGE 1-B



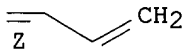
RN 184291-62-1 CAPLUS
CN 2H-Pyran-2-one, 6-[12-(acetyloxy)-14-[(aminocarbonyl)oxy]-2,6-dihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, [3R-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11S*,12R*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



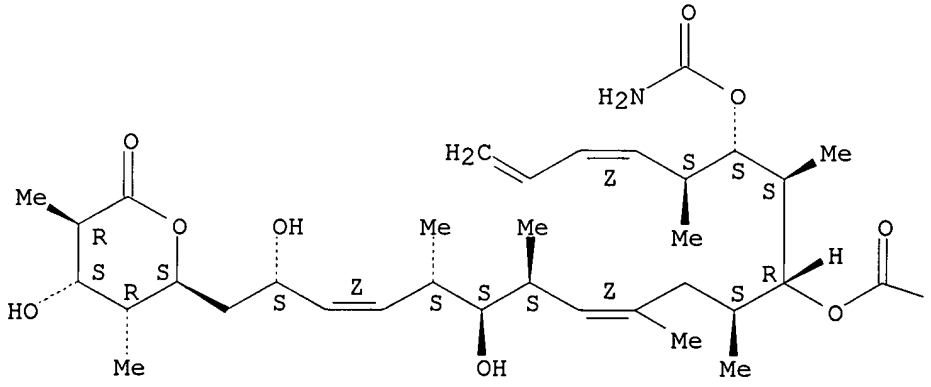
PAGE 1-B



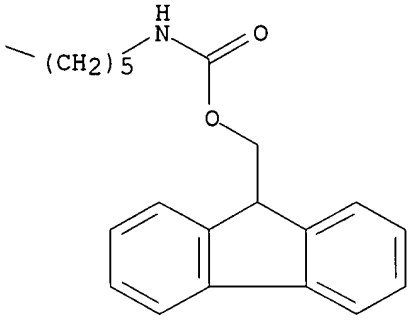
RN 184291-68-7 CAPLUS
CN Hexanoic acid, 6-[[(9H-fluoren-9-ylmethoxy)carbonyl]amino]-, 1-[2-[(aminocarbonyl)oxy]-1,3-dimethyl-4,6-heptadienyl]-7,11-dihydroxy-2,4,6,8-tetramethyl-12-(tetrahydro-4-hydroxy-3,5-dimethyl-6-oxo-2H-pyran-2-yl)-4,9-dodecadienyl ester, [2S-[2.alpha.[1S*(1R*,2R*,3R*,4Z),2R*,4Z,6R*,7R*,8R*,9Z,11R*],3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



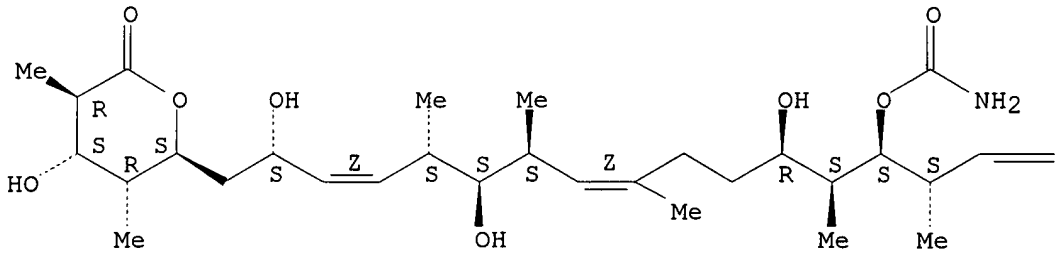
PAGE 1-B



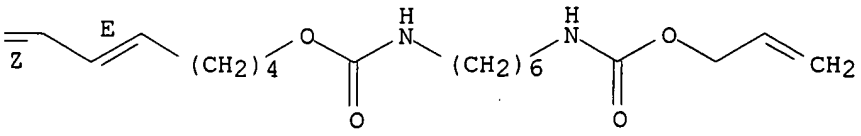
RN 184291-80-3 CAPLUS
CN Carbamic acid, [6-[[[[10-[(aminocarbonyl)oxy]-12,18,22-trihydroxy-9,11,15,17,19-pentamethyl-23-(tetrahydro-4-hydroxy-3,5-dimethyl-6-oxo-2H-pyran-2-yl)-5,7,15,20-tricosatetraenyl]oxy]carbonyl]amino]hexyl]-, 2-propenyl ester, [2S-[2.alpha.(5E,7E,9R*,10R*,11R*,12S*,15Z,17R*,18R*,19R*,20Z,22R*),3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

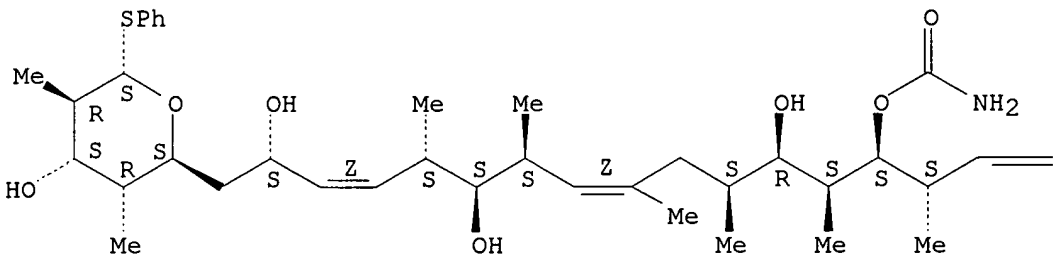


RN 184291-81-4 CAPLUS
CN 3,8,16,18-Nonadecatetraene-2,6,12,14-tetrol, 5,7,9,11,13,15-hexamethyl-1-

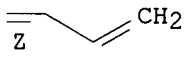
[tetrahydro-4-hydroxy-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-, 14-carbamate, [2S-[2.alpha.(2R*,3Z,5R*,6R*,7R*,8Z,11R*,12S*,13R*,14R*,15R*,16Z),3.beta.,4.beta.,5.alpha.,6.beta.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



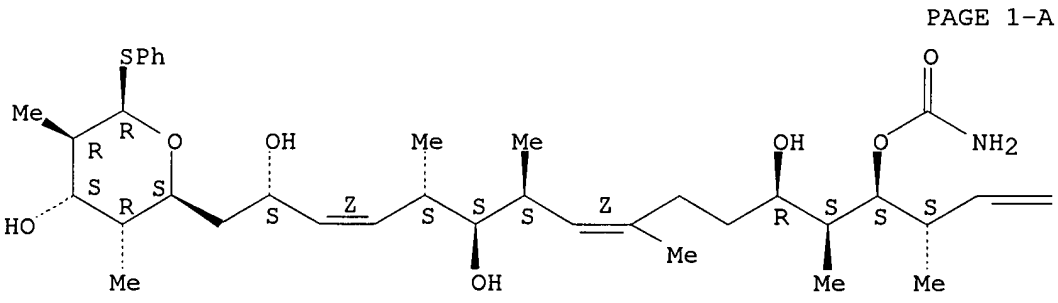
PAGE 1-B



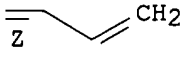
RN 184291-82-5 CAPLUS
CN 3,8,16,18-Nonadecatetraene-2,6,12,14-tetrol, 5,7,9,13,15-pentamethyl-1-[tetrahydro-4-hydroxy-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-, 14-carbamate, [2S-[2.alpha.(2R*,3Z,5R*,6R*,7R*,8Z,12S*,13R*,14R*,15R*,16Z),3.beta.,4.beta.,5.alpha.,6.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



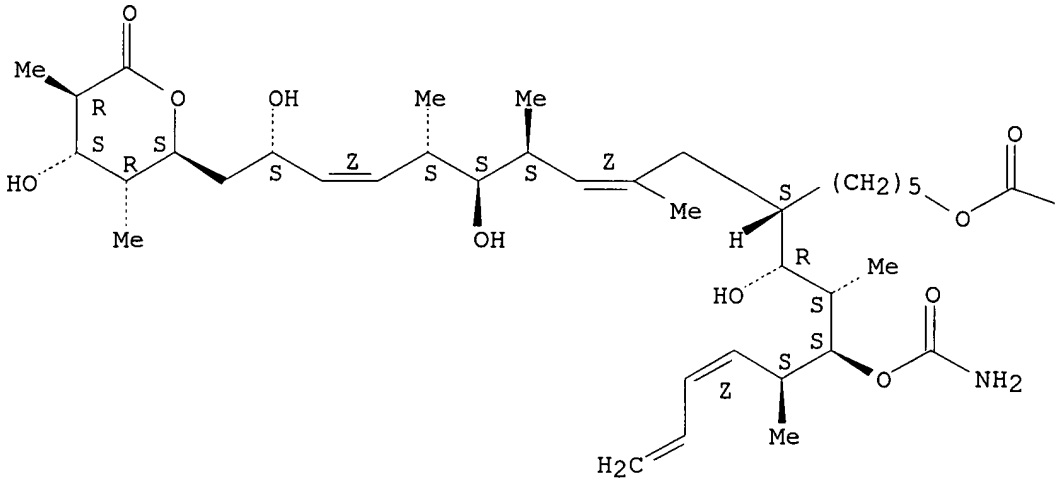
PAGE 1-B



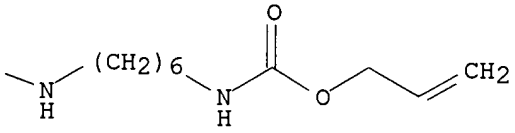
RN 184291-90-5 CAPLUS
CN Carbamic acid, [6-[[[[6-[3-[(aminocarbonyl)oxy]-1-hydroxy-2,4-dimethyl-5,7-octadienyl]-11,15-dihydroxy-8,10,12-trimethyl-16-(tetrahydro-4-hydroxy-3,5-dimethyl-6-oxo-2H-pyran-2-yl)-8,13-hexadecadienyl]oxy]carbonyl]amino]hexyl]-, 2-propenyl ester, [2S-[2.alpha.[6R*(1S*,2R*,3R*,4R*,5Z),8Z,10R*,11R*,12R*,13Z,15R*],3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



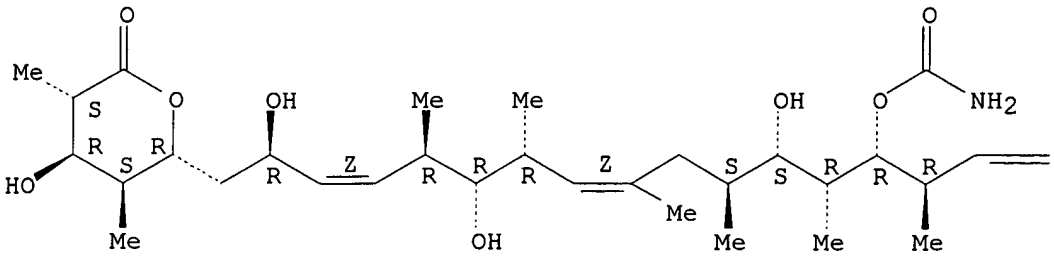
PAGE 1-B



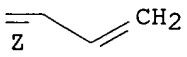
RN 184488-81-1 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11R*,12R*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



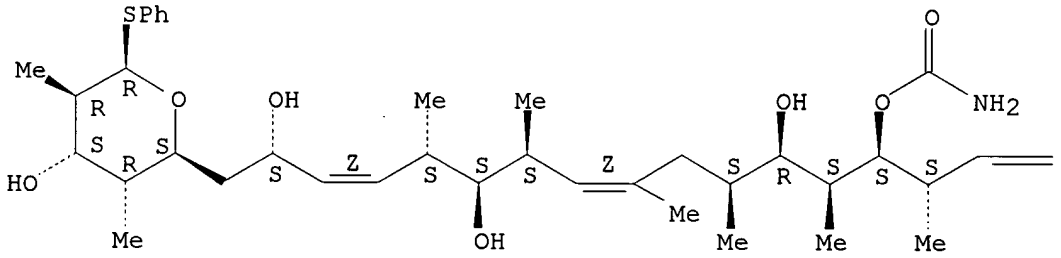
PAGE 1-B



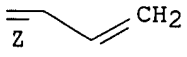
RN 184488-83-3 CAPLUS
CN 3,8,16,18-Nonadecatetraene-2,6,12,14-tetrol, 5,7,9,11,13,15-hexamethyl-1-[tetrahydro-4-hydroxy-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-, 14-carbamate, [2S-[2.alpha.(2R*,3Z,5R*,6R*,7R*,8Z,11R*,12S*,13R*,14R*,15R*,16Z),3.beta.,4.beta.,5.alpha.,6.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



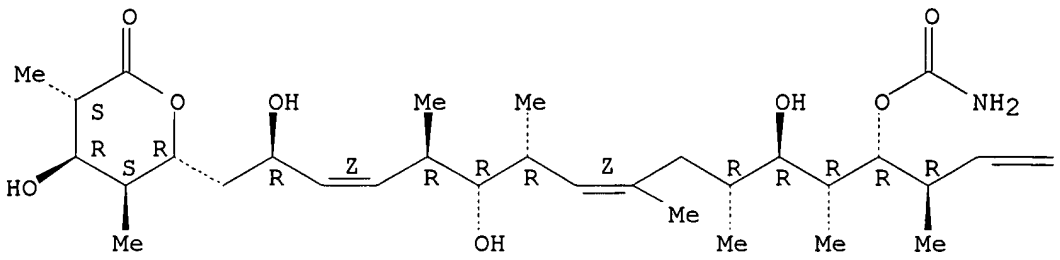
PAGE 1-B



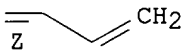
RN 184777-96-6 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11S*,12S*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



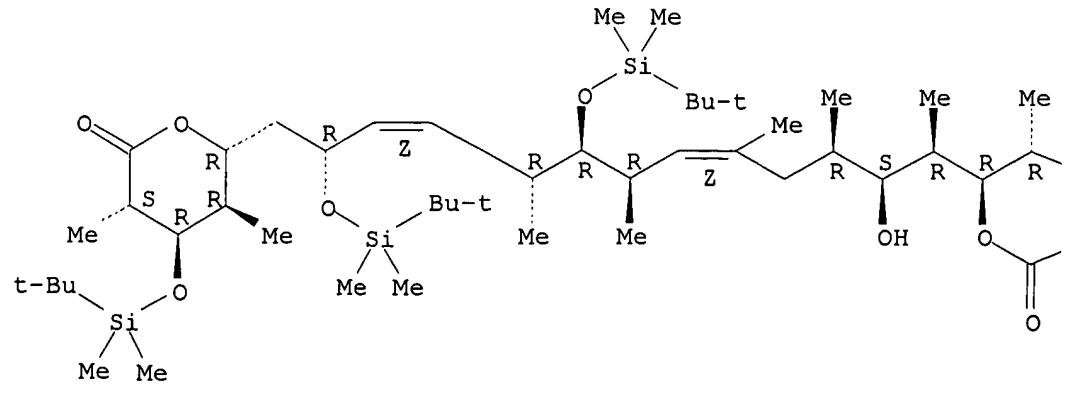
IT **153788-99-9P 184291-44-9P 184291-45-0P**
184291-75-6P 184291-76-7P 184291-79-0P
184291-83-6P 184291-89-2P 184292-32-8P
184292-34-0P 184292-36-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(syntheses of discodermolides useful for investigating microtubule binding and stabilization)

RN 153788-99-9 CAPLUS

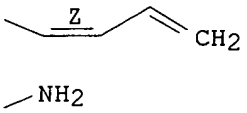
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11S*,12R*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



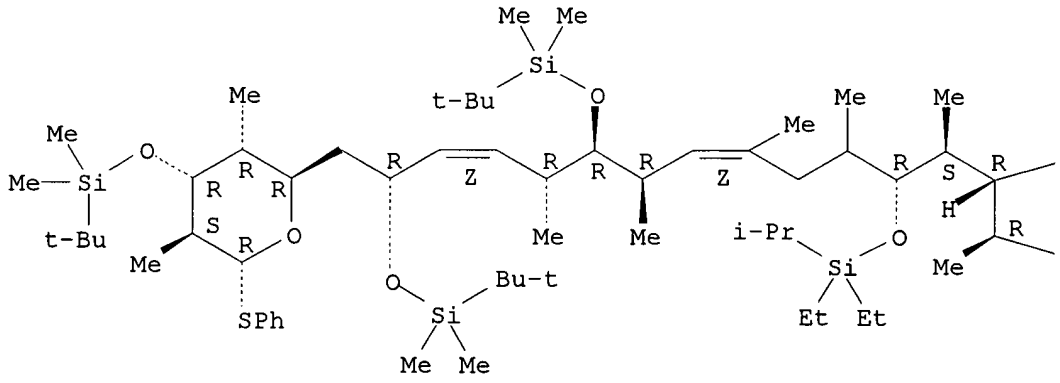
PAGE 1-B



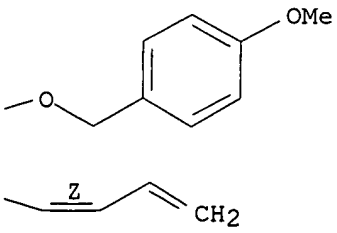
RN 184291-44-9 CAPLUS
CN 4,16-Dioxa-3,17-disilanonadeca-6,11-diene, 9-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5-[[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]methyl]-17,17-diethyl-15-[2-[(4-methoxyphenyl)methoxy]-1,3-dimethyl-4,6-heptadienyl]-2,2,8,10,12,14,18-heptamethyl-, [2R-[2.alpha.[5R*,6Z,8R*,9R*,10R*,11Z,15R*(1S*,2R*,3R*,4Z)],3.beta.,4.beta.,5.alpha.,6.beta.]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



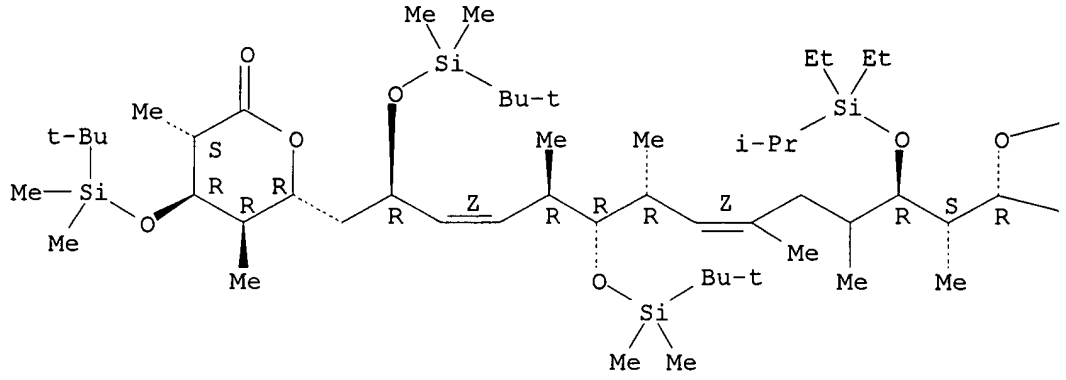
PAGE 1-B



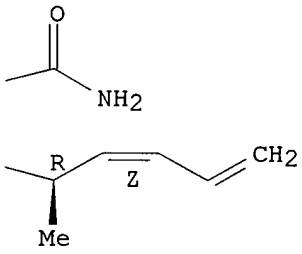
RN 184291-45-0 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-12-[[diethyl(1-methylethyl)silyl]oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,12S*,13R*,14S*,15S*,16Z)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



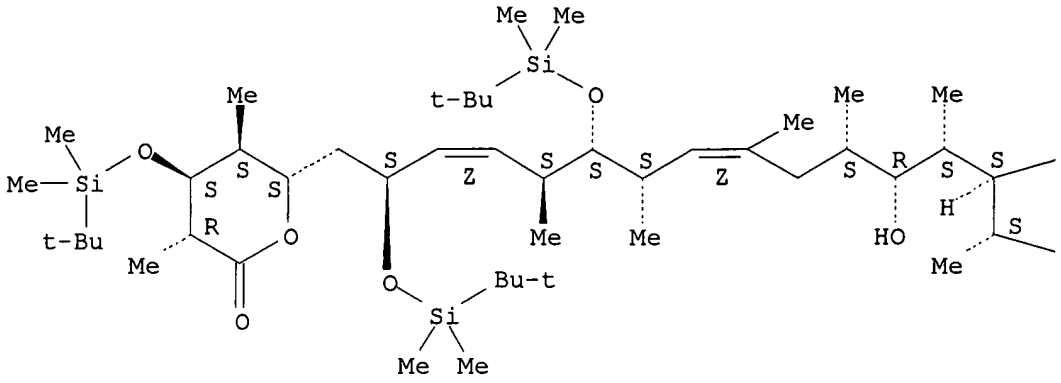
PAGE 1-B



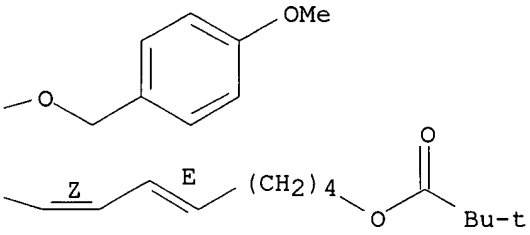
RN 184291-75-6 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, 18,22-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-23-[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-oxo-2H-pyran-2-yl]-12-hydroxy-10-[(4-methoxyphenyl)methoxy]-9,11,13,15,17,19-hexamethyl-5,7,15,20-tricosatetraenyl ester, [2S-[2.alpha.(5E,7Z,9R*,10R*,11S*,12S*,13R*,15Z,17R*,18R*,19R*,20Z,22R*),3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



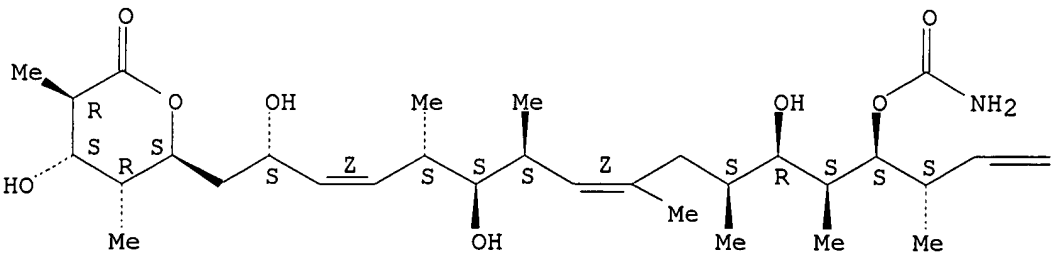
PAGE 1-B



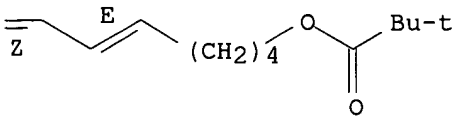
RN 184291-76-7 CAPLUS
CN Propanoic acid, 2,2-dimethyl-, 10-[(aminocarbonyl)oxy]-12,18,22-trihydroxy-9,11,13,15,17,19-hexamethyl-23-(tetrahydro-4-hydroxy-3,5-dimethyl-6-oxo-2H-pyran-2-yl)-5,7,15,20-tricosatetraenyl ester, [2S-[2.alpha.(5E,7Z,9R*,10R*,11R*,12S*,13R*,15Z,17R*,18R*,19R*,20Z,22R*),3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



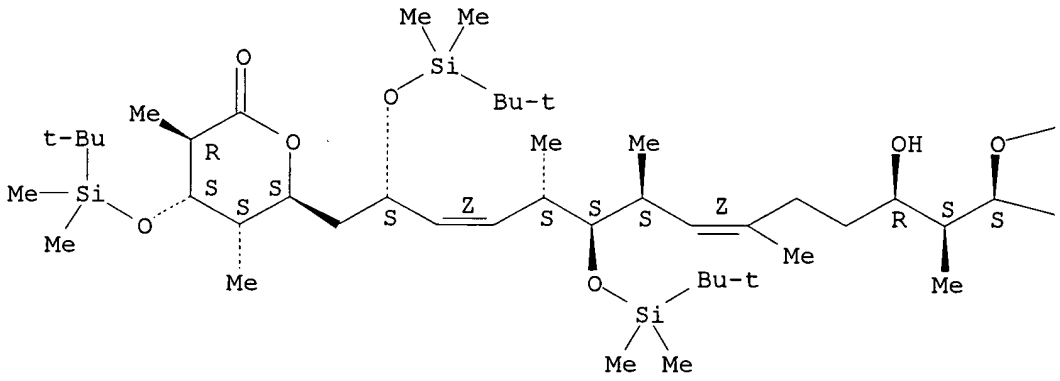
PAGE 1-B



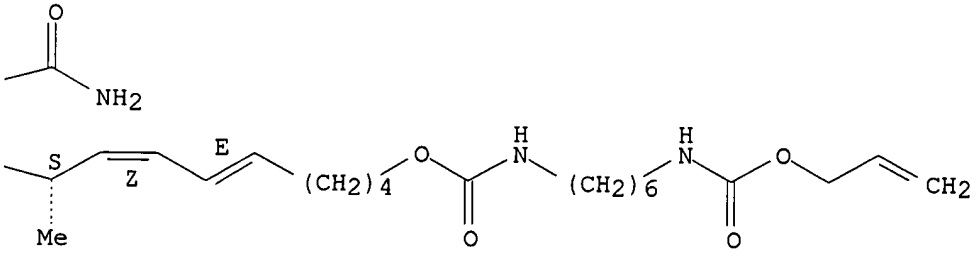
RN 184291-79-0 CAPLUS
CN 11,34-Dioxa-2,9-diaza-35-silaheptatriaconta-16,18,26,31-tetraenoic acid, 21-[(aminocarbonyl)oxy]-29-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-33-[[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-oxo-2H-pyran-2-yl]methyl]-23-hydroxy-20,22,26,28,30,35,35,36,36-nonamethyl-10-oxo-, 2-propenyl ester, [2S-[2.alpha.(16E,18Z,20R*,21R*,22R*,23S*,26Z,28R*,29R*,30R*,31Z,33R*),3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

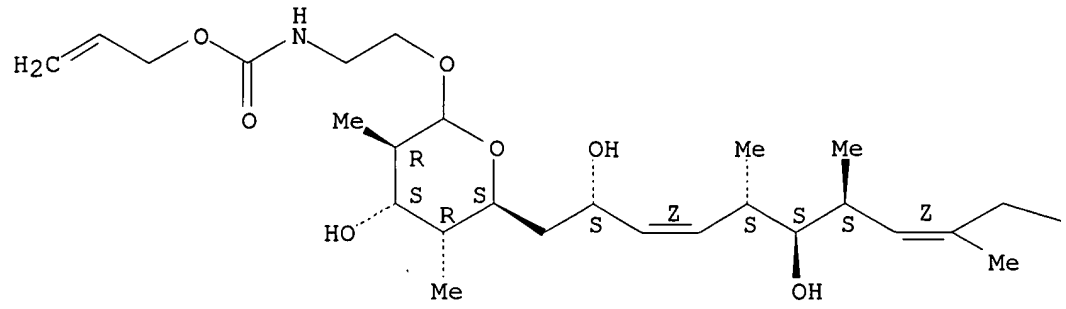


RN 184291-83-6 CAPLUS
CN Carbamic acid, [2-[[6-[14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,13,15-pentamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-2H-pyran-2-yl]oxy]ethyl]-, 2-propenyl ester,

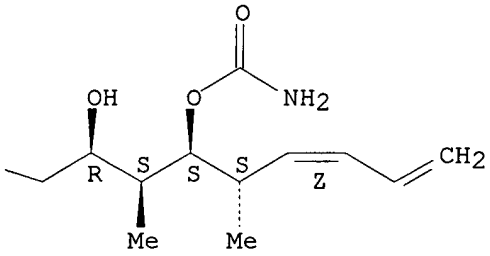
[3R,4S,5R,6S(2S,3Z,5S,6S,7S,8Z,12R,13S,14S,15S,16Z)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



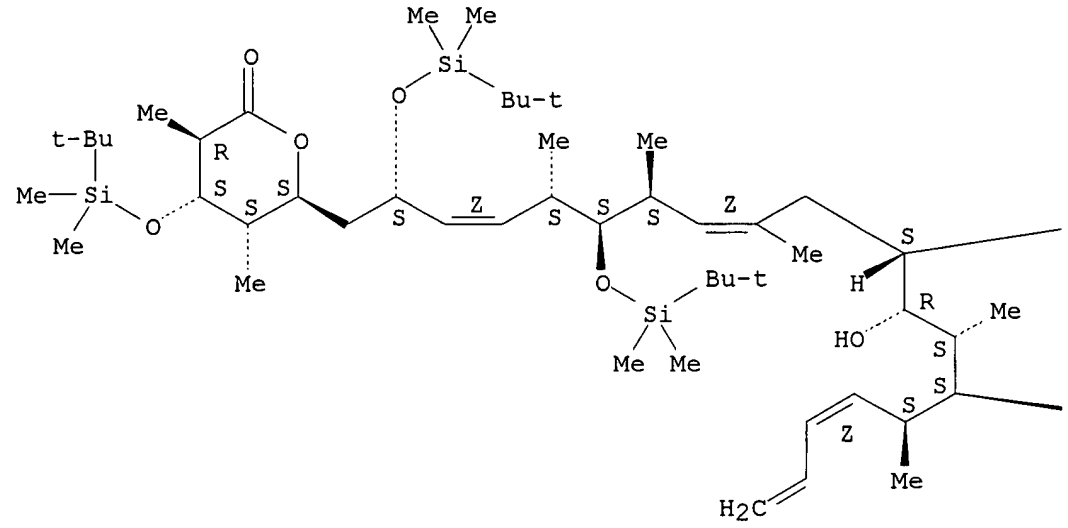
PAGE 1-B



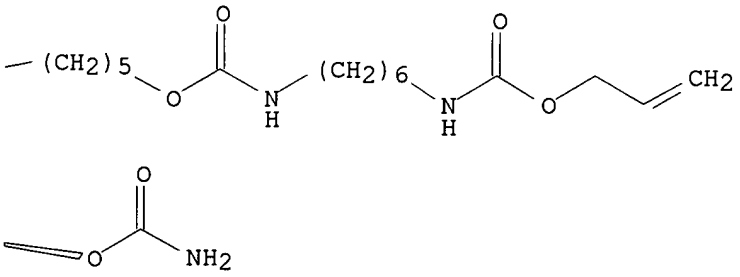
RN 184291-89-2 CAPLUS
CN 11,27-Dioxa-2,9-diaza-28-silatriaconta-19,24-dienoic acid, 17-[3-[(aminocarbonyl)oxy]-1-hydroxy-2,4-dimethyl-5,7-octadienyl]-22-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-26-[[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-oxo-2H-pyran-2-yl]methyl]-19,21,23,28,28,29,29-heptamethyl-10-oxo-, 2-propenyl ester, [2S-[2.alpha.[17R*(1S*,2R*,3R*,4R*,5Z),19Z,21R*,22R*,23R*,24Z,26R*],3.beta.,4.beta.,5.alpha.]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



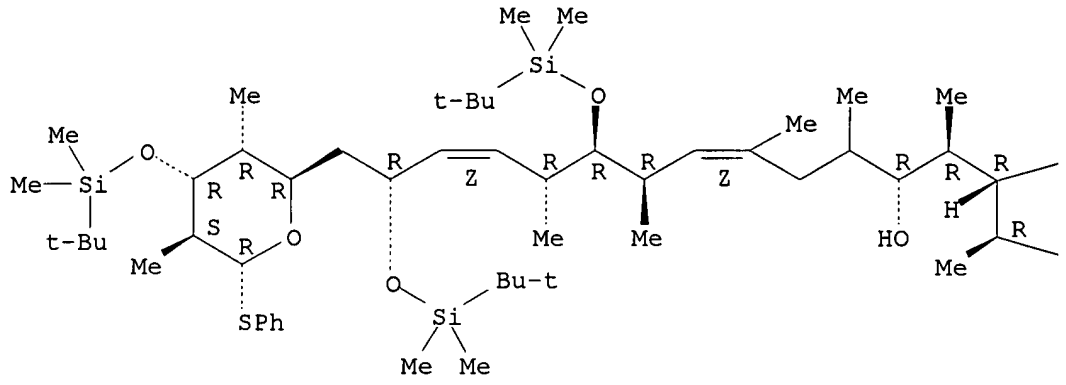
PAGE 1-B



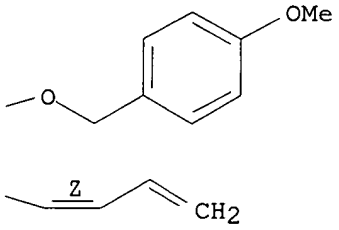
RN 184292-32-8 CAPLUS
CN 1,3,11,16-Nonadecatetraen-8-ol, 14,18-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-19-[4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-6-(phenylthio)-2H-pyran-2-yl]-6-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-, [2R-[2.alpha.(3Z,5R*,6R*,7R*,8R*,11Z,13R*,14R*,15R*,16Z,18R*),3.beta.,4.beta.,5.alpha.,6.beta.]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



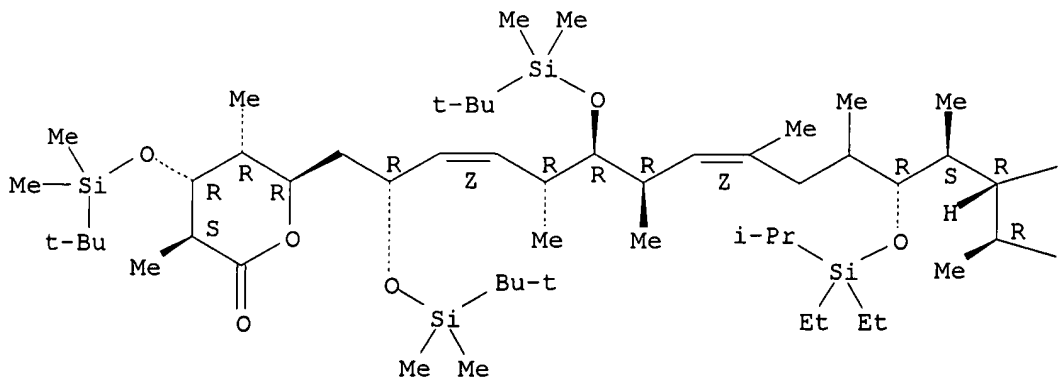
PAGE 1-B



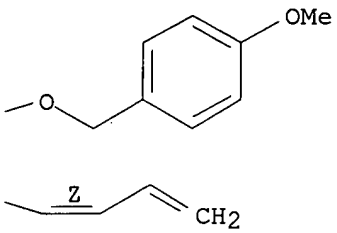
RN 184292-34-0 CAPLUS
CN 2H-Pyran-2-one, 6-[12-[[diethyl(1-methylethyl)silyl]oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-[(4-methoxyphenyl)methoxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,12S*,13R*,14S*,15S*,16Z)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



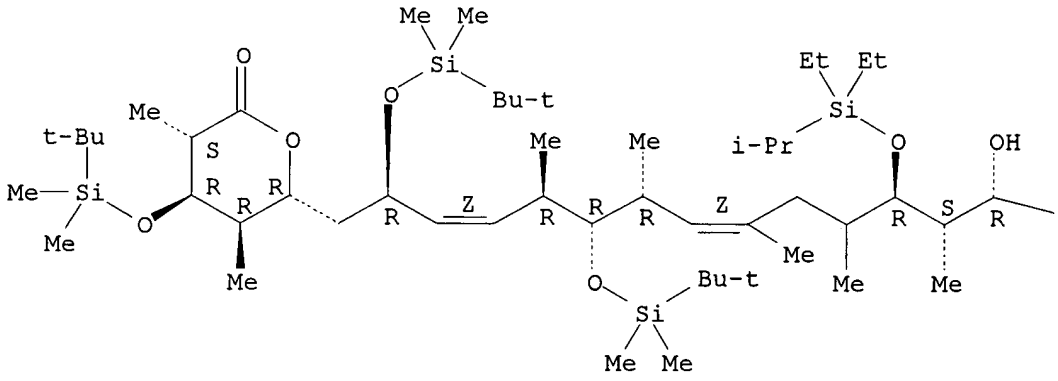
PAGE 1-B



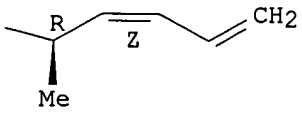
RN 184292-36-2 CAPLUS
CN 2H-Pyran-2-one, 6-[12-[[diethyl(1-methylethyl)silyl]oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-14-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,12S*,13R*,14S*,15S*,16Z)]]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



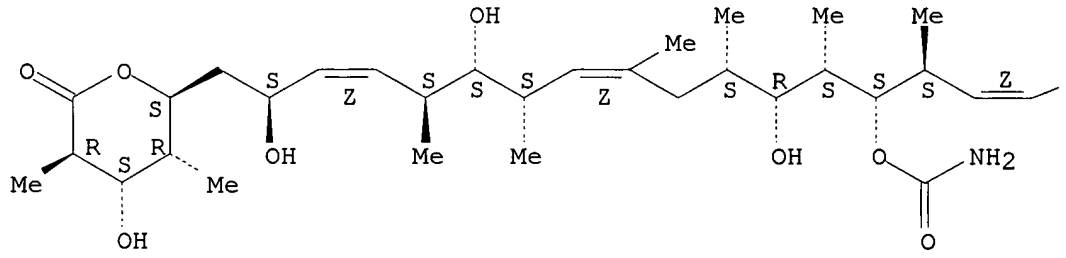
PAGE 1-B



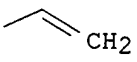
L4 ANSWER 90 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:408067 CAPLUS
DOCUMENT NUMBER: 125:131838
TITLE: Computational and biochemical analysis of three novel anticancer drugs: Z-1,1-dichloro-2,3-diphenylcyclopropane, Z-chlorochalcone and (+)-discodermolide (taxol)
AUTHOR(S): Ter Haar, Ernst
CORPORATE SOURCE: Univ. of Pittsburgh, Pittsburgh, PA, USA
SOURCE: (1995) 208 pp. Avail.: Univ. Microfilms Int., Order No. DA9614160
From: Diss. Abstr. Int., B 1996, 57(1), 261
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7**, (+)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(computational and biochem. anal. of three novel anticancer drugs chlorophenylcyclopropane and chlorochalcone and discodermolide (taxol))
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 91 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:306243 CAPLUS
DOCUMENT NUMBER: 125:836
TITLE: (+)-Discodermolide binds to microtubules in stoichiometric ratio to tubulin dimers, blocks taxol binding and results in mitotic arrest
AUTHOR(S): Hung, Deborah T.; Chen, Jie; Schreiber, Stuart L.
CORPORATE SOURCE: Howard Hughes Med. Inst., Harvard Univ., Cambridge, MA, 02138, USA

SOURCE: Chemistry & Biology (1996), 3(4), 287-293
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: The marine natural product (+)-discodermolide has potent immunosuppressive activity. It inhibits proliferation of a wide range of human and murine cells, induces cell cycle arrest in the G2 or M phase and was recently shown to stabilize microtubules. Total synthesis of discodermolide has made it possible to generate variants of the compd. to study its intracellular function in detail. Results: We have detd. that (+)-discodermolide arrests MG63 cells at M phase, and has a stabilizing effect on microtubules. In vitro studies show that discodermolide induces polymn. of purified tubulin in the absence of microtubule-assocd. proteins, and that it binds to tubulin dimers in microtubules at 1:1 stoichiometry. Discodermolide binds taxol-polymd. microtubules at near stoichiometric level, whereas taxol binds discodermolide-induced microtubules poorly. Competition data show that the binding of microtubules by discodermolide and taxol are mutually exclusive; discodermolide binds with higher affinity than taxol. The results of binding assays carried out in vivo or in cell lysates also suggest that the microtubule network is discodermolide's cellular target. Conclusions: (+)-Discodermolide causes cell cycle arrest at the metaphase-anaphase transition in mitosis, presumably due to its stabilizing effect on microtubules. In vitro, discodermolide polymerizes purified tubulin potently in the absence of MAPs. It binds microtubules at one mol. per tubulin dimer with a higher affinity than taxol, and the binding of microtubules by discodermolide and taxol are mutually exclusive. In total cell lysates discodermolide displays binding activity that is consistent with its effects on microtubules.

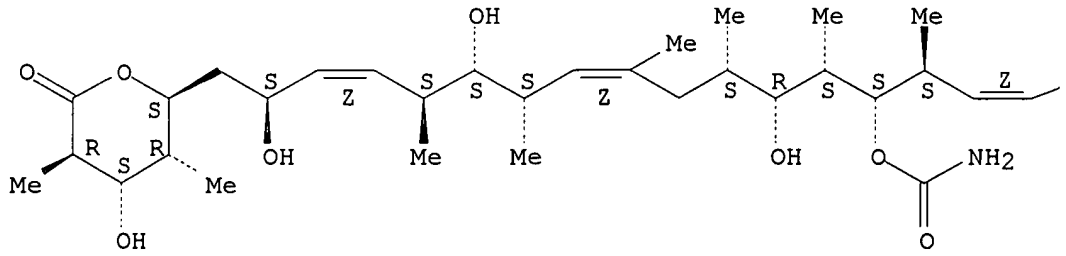
IT **127943-53-7**, (+)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
((+)-Discodermolide binds to microtubules in stoichiometric ratio to tubulin dimers, blocks taxol binding and results in mitotic arrest)

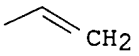
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





L4 ANSWER 92 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:991222 CAPLUS
DOCUMENT NUMBER: 124:45042
TITLE: Discodermolide, A Cytotoxic Marine Agent That Stabilizes Microtubules More Potently Than Taxol
AUTHOR(S): ter Haar, Ernst; Kowalski, Richard J.; Hamel, Ernest; Lin, Chii M.; Longley, Ross E.; Gunasekera, Sarath P.; Rosenkranz, Herbert S.; Day, Billy W.
CORPORATE SOURCE: Department of Environmental and Occupational Health, University of Pittsburgh, Pittsburgh, PA, 15238, USA
SOURCE: Biochemistry (1996), 35(1), 243-50
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

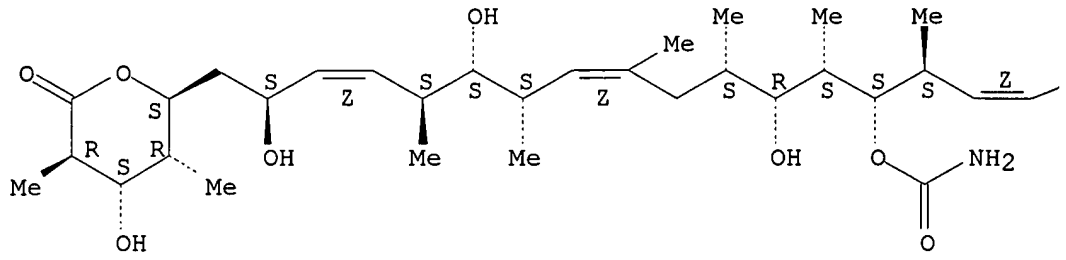
AB Computer-assisted structure anal. indicated (+)-discodermolide, a polyhydroxylated alkatetraene lactone marine natural product, was an antimitotic compd., and we confirmed this prediction. Previous work had shown an accumulation of discodermolide-treated cells in the G2/M portion of the cell cycle, and we have now found that discodermolide arrests Burkitt lymphoma cells in mitosis. Discodermolide-treated breast carcinoma cells displayed spectacular rearrangement of the microtubule cytoskeleton, including extensive microtubule bundling. Microtubule rearrangement that occurred with 10 nM discodermolide required 1 .mu.M taxol. Discodermolide had equally impressive effects on tubulin assembly in vitro. Near-total polymn. occurred at 0 .degree.C with tubulin plus microtubule-assocd. proteins (MAPs) under conditions in which taxol at an identical concn. was inactive. Without MAPs and/or without GTP, tubulin assembly was also more vigorous with discodermolide than with taxol under every reaction condition examd. Discodermolide-induced polymer differed from taxol-induced polymer in that it was completely stable at 0 .degree.C in the presence of high concns. of Ca2+. In a quant. assay designed to select for agents more effective than taxol in inducing assembly, discodermolide had an EC50 value of 3.2 .mu.M vs. 23 .mu.M for taxol.

IT **127943-53-7**, (+)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(discodermolide stabilization of microtubules)

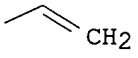
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

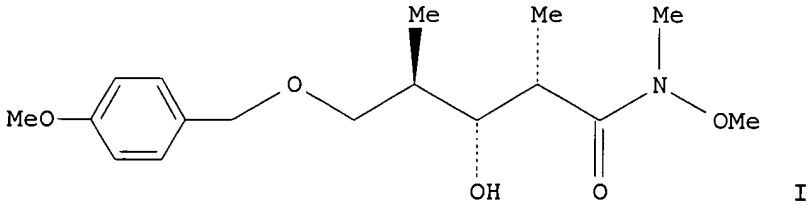


PAGE 1-B



L4 ANSWER 93 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:938846 CAPLUS
DOCUMENT NUMBER: 124:86679
TITLE: Total Synthesis of (-)-Discodermolide
AUTHOR(S): Smith, Amos B., III; Qiu, Yuping; Jones, David R.; Kobayashi, Kaoru
CORPORATE SOURCE: Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, PA, 19104, USA
SOURCE: Journal of the American Chemical Society (1995), 117(48), 12011-12
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 124:86679
GI



I

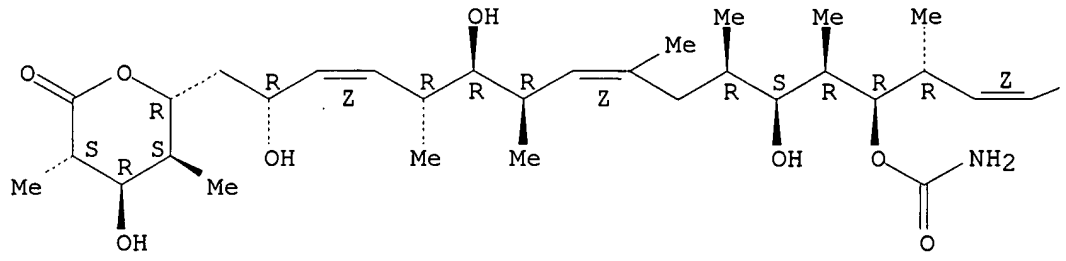
AB A highly convergent and stereoselective total synthesis of (-)-discodermolide, antipode of the potent immunosuppressant (+)-discodermolide, has been achieved. The cornerstone of the successful strategy was elaboration of three fragments from common precursor (+)-I, the latter contg. the repeating stereochem. triad of the discodermolide backbone. Final assembly of the target then exploited a combination of .sigma.- and .pi.-bond constructions of the olefinic linkages.

IT **154335-30-5P**, (-)-Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of (-)-discodermolide)

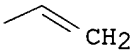
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



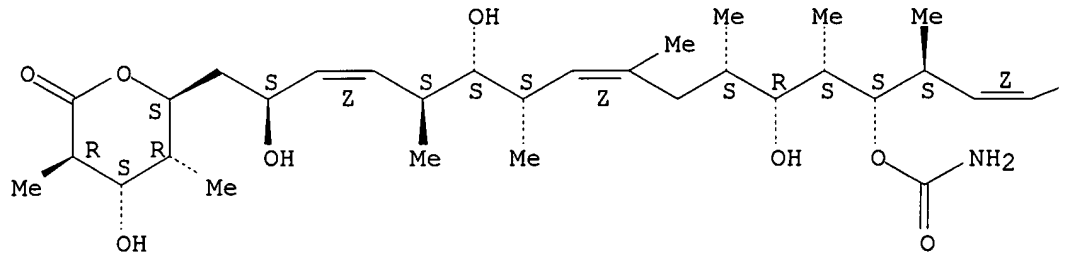
PAGE 1-B



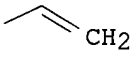
L4 ANSWER 94 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:654555 CAPLUS
DOCUMENT NUMBER: 123:82974
TITLE: Total synthesis of the immunosuppressive agent (-)-discodermolide. Distinct binding and cellular properties of synthetic (+)- and (-)-discodermolide
AUTHOR(S): Stafford, Jeffrey A.; Mehrotra, Mukund M.
CORPORATE SOURCE: Glaxo Research Institute, USA
SOURCE: Chemtracts: Organic Chemistry (1995), 8(1), 41-7
CODEN: CMOCEI; ISSN: 0895-4445
PUBLISHER: Data Trace Chemistry Publishers, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB The title research of J.B. Nerenberg et al. (1993) and D.T. Hung et al. (1994) is reviewed with commentary and 9 refs.
IT **127943-53-7**, (+)-Discodermolide **154335-30-5**, (-)-Discodermolide
RL: MSC (Miscellaneous)
(total synthesis of discodermolide and distinct binding and cellular properties)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



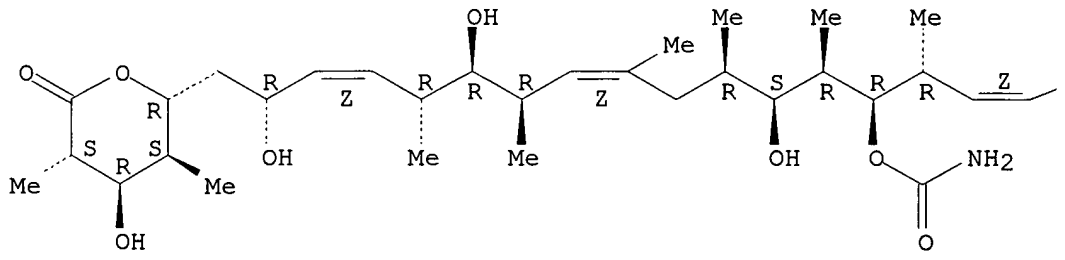
PAGE 1-B



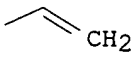
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

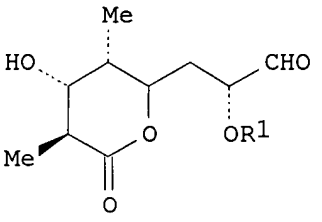


L4 ANSWER 95 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:615210 CAPLUS
DOCUMENT NUMBER: 123:32864
TITLE: Total synthesis of discodermolide
INVENTOR(S): Golec, Julian Marian Charles; Jones, Stuart Donald; Gillespie, Roger John
PATENT ASSIGNEE(S): Roussel Laboratories Ltd., UK
SOURCE: Brit. UK Pat. Appl., 57 pp.

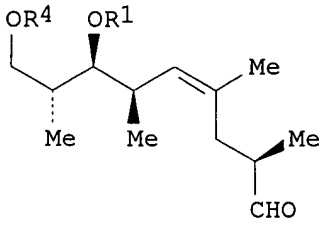
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2280677	A1	19950208	GB 1994-15399	19940729
GB 2280677	B2	19970924		

PRIORITY APPLN. INFO.: GB 1993-15802 19930730
GI



I



II

AB Novel compds., pyranone I (R1 = protecting group) and alkenal II (R1, R4 = protecting group) and the enantiomeric and diastereoisomeric forms thereof are disclosed as are methods for their prepn. and novel intermediates used in such methods. Their use in the total synthesis of discodermolide (III) and enantiomeric and diastereoisomeric forms thereof is disclosed. Also claimed are various intermediates prepd. in synthesizing III from I and II.

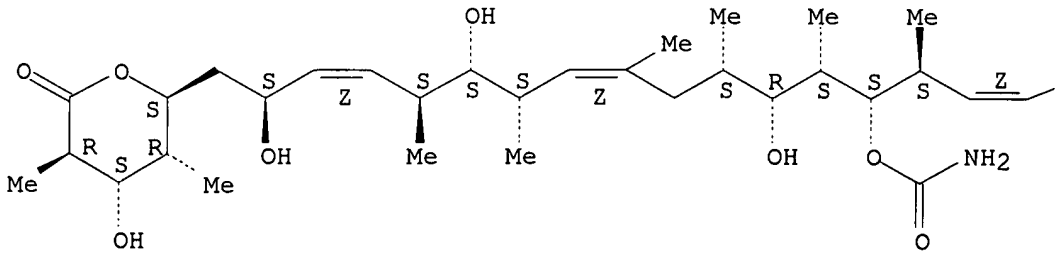
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(total synthesis of discodermolide)

RN 127943-53-7 CAPLUS

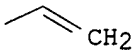
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



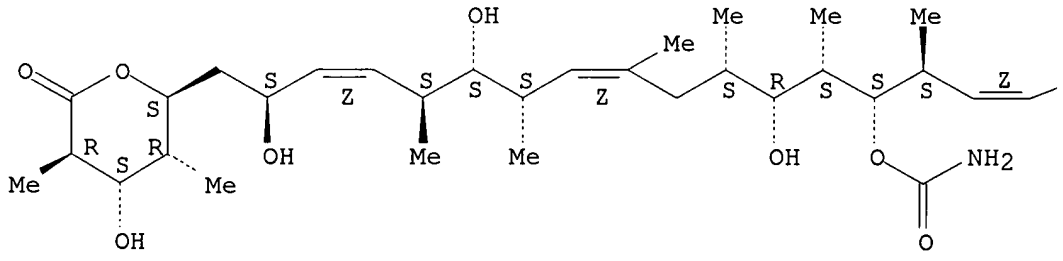
PAGE 1-B



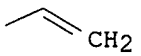
L4 ANSWER 96 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:607006 CAPLUS
DOCUMENT NUMBER: 123:169415
TITLE: Studies toward the total synthesis of discodermolide: the C-9 to C-24 fragment
AUTHOR(S): Yang, Ge
CORPORATE SOURCE: Univ. of California, Los Angeles, CA, USA
SOURCE: (1994) 189 pp. Avail.: Univ. Microfilms Int., Order No. DA9511125
From: Diss. Abstr. Int. B 1995, 55(11), 4859
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable
IT **127943-53-7DP**, Discodermolide, C(9)-C(24) fragment
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a discodermolide fragment)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 97 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:439873 CAPLUS
DOCUMENT NUMBER: 123:56196
TITLE: Reactivity of (pentadienyl)iron(1+) cations: effect of

peripheral ligands on the regioselectivity of nucleophilic addition
AUTHOR(S): Donaldson, William A.; Shang, Lewei
CORPORATE SOURCE: Department of Chemistry, Marquette Univ., Milwaukee, WI, 53233, USA
SOURCE: Tetrahedron Letters (1995), 36(10), 1575-6
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:56196

AB Nucleophilic addn. to the (1-methylpentadienyl)Fe(CO)2PPh3+ cation proceeds predominantly at the substituted pentadienyl terminus to afford (5-substituted-1,3-(Z)-hexadiene)Fe(CO)2PPh3 products in very good yields. Decomplexation with Ce4+ generates the free ligand in good yields.

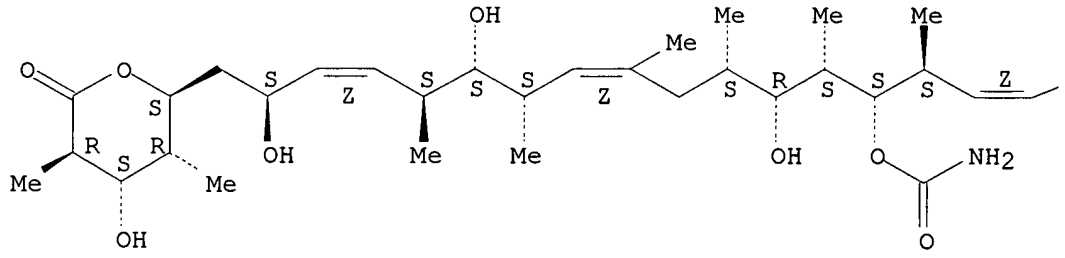
IT **127943-53-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 127943-53-7 CAPLUS

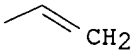
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

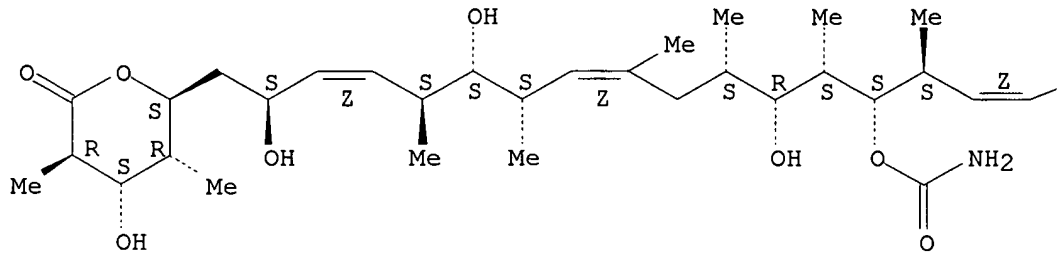


L4 ANSWER 98 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:407018 CAPLUS
DOCUMENT NUMBER: 122:214310
TITLE: I. Synthetic and mechanistic studies of the Daphniphyllum alkaloids. II. Progress towards the C1-C3 fragment of discodermolide
AUTHOR(S): Kath, John Charles
CORPORATE SOURCE: Univ. California, Berkeley, CA, USA
SOURCE: (1993) 210 pp. Avail.: Univ. Microfilms Int., Order No. DA9430557
From: Diss. Abstr. Int. B 1995, 55(7), 2733
DOCUMENT TYPE: Dissertation

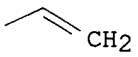
LANGUAGE: English
AB Unavailable
IT **127943-53-7P**, Discodermolide
RL: PNU (Preparation, unclassified); PREP (Preparation)
(synthesis of C1-C3 fragment of discodermolide)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L4 ANSWER 99 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:172225 CAPLUS
DOCUMENT NUMBER: 122:23777
TITLE: Distinct binding and cellular properties of synthetic (+)- and (-)-discodermolides
AUTHOR(S): Hung, Deborah T.; Nerenberg, Jennie B.; Schreiber, Stuart L.
CORPORATE SOURCE: Department of Chemistry, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Chemistry & Biology (1994), 1(1), 67-71
CODEN: CBOLE2; ISSN: 1074-5521
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The (+)- and (-)-enantiomers of the marine natural product discodermolide were prepd. by total synthesis (general synthetic schemes given). Both enantiomers had antiproliferative activity on cultured cells, but they acted by distinct mechanisms and appeared to have distinct cellular targets. The natural product, the (+)-enantiomer, blocked the cell cycle in the G2 or M phase. The (-)-enantiomer blocked cells in the S phase. A specific binding activity was identified for (+)-discodermolide, and evidence is provided that it interacts with a functionally relevant receptor. No such specific binding was found for (-)-discodermolide, and the binding of the 2 isomers was not competitive.
IT **127943-53-7P 154335-30-5P**, (-)-Discodermolide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

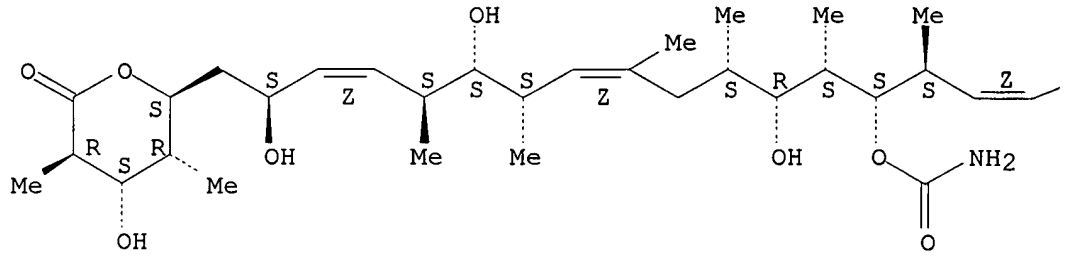
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and biol. activities of)

RN 127943-53-7 CAPLUS

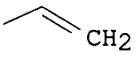
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

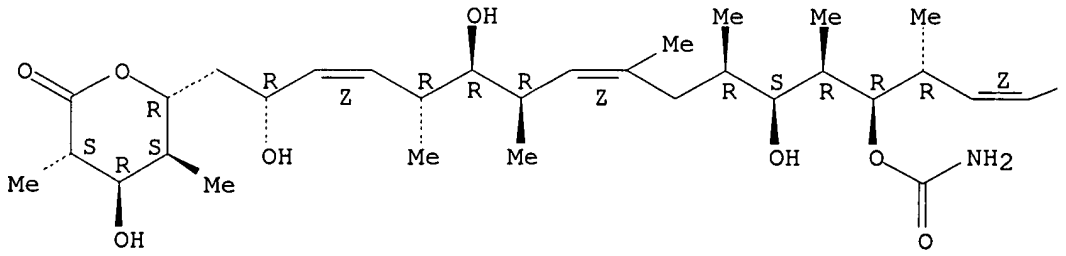


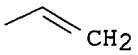
RN 154335-30-5 CAPLUS

CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

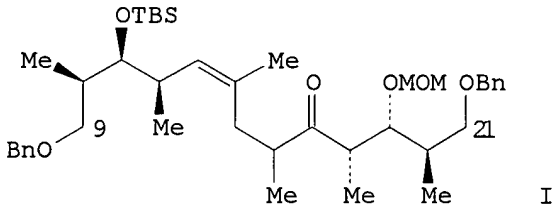
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

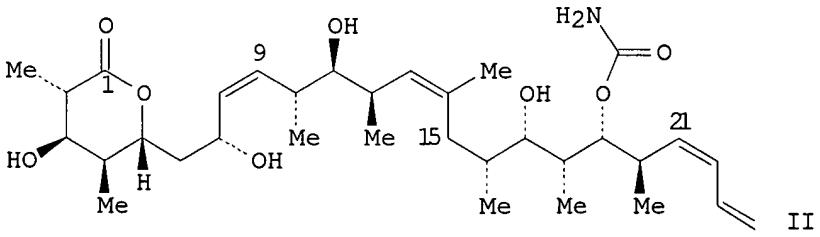




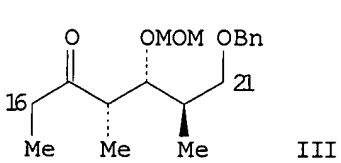
L4 ANSWER 100 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:680450 CAPLUS
DOCUMENT NUMBER: 121:280450
TITLE: The synthesis of the C-9 to C-21 sector of discodermolide: an efficient route to the C13-14 Z-trisubstituted alkene
AUTHOR(S): Yang, Ge; Myles, David C.
CORPORATE SOURCE: Dep. Chem. Biochem., UCLA, Los Angeles, CA, 90024-1569, USA
SOURCE: Tetrahedron Letters (1994), 35(16), 2503-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:280450
GI



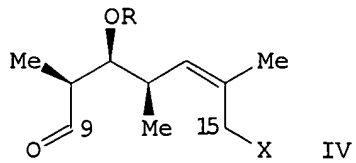
I



II



III



IV

AB The synthesis of the C-9 to C-21 sector I of the immunosuppressive marine natural product discodermolide (II) is described. The C-9 to C-15 subunit subunit is synthesized in five steps from aldehyde, (R)-PhCH2OCH2CHMeCHO using the diene aldehyde cyclocondensation reaction. Diastereoselective alkylation of the previously synthesized C-16 to C-21 III subunit by a suitably functionalized C-9 to C-15 synthon IV leads to the C-9 to C-21

sector I of II.

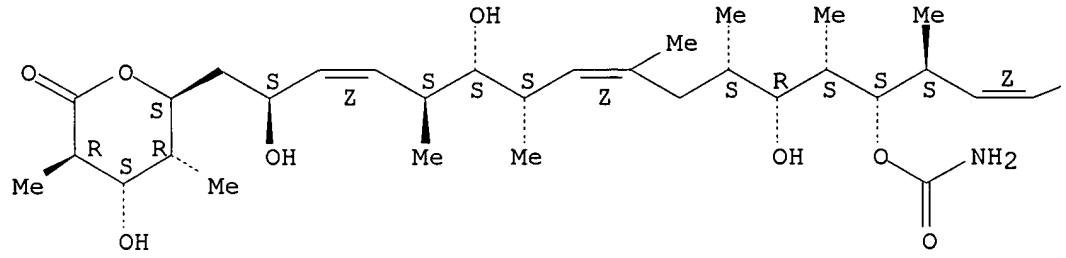
IT **127943-53-7**, Discodermolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(chiral building block for, prepn. of)

RN 127943-53-7 CAPLUS

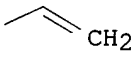
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

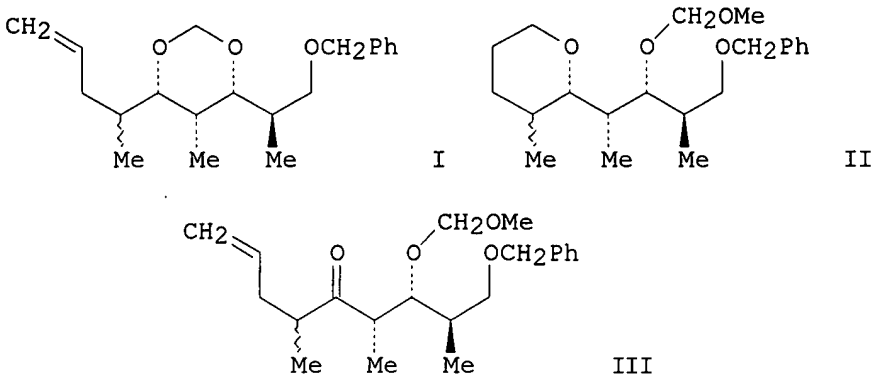


PAGE 1-B



L4 ANSWER 101 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:508336 CAPLUS
DOCUMENT NUMBER: 121:108336
TITLE: An alkylative strategy to the C-13 to C-21 sector of discodermolide
AUTHOR(S): Yang, Ge; Myles, David C.
CORPORATE SOURCE: Dep. Chem. Biochem., UCLA, Los Angeles, CA, 90024-1569, USA
SOURCE: Tetrahedron Letters (1994), 35(9), 1313-16
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 121:108336
GI



AB The triols I and II were prepd. as an approach to the C(13)-C(21) sector of the immunosuppressive marine natural product discodermolide. The C(15)-C(16) bond is formed by diastereoselective alkylation of a ketone enolate. Either diastereomer of the alkylation product III can be obtained by selecting the appropriate counter ion. The C(16)-C(21) subunit is prepd. in two steps from (R)-PhCH2CHMeCHO.

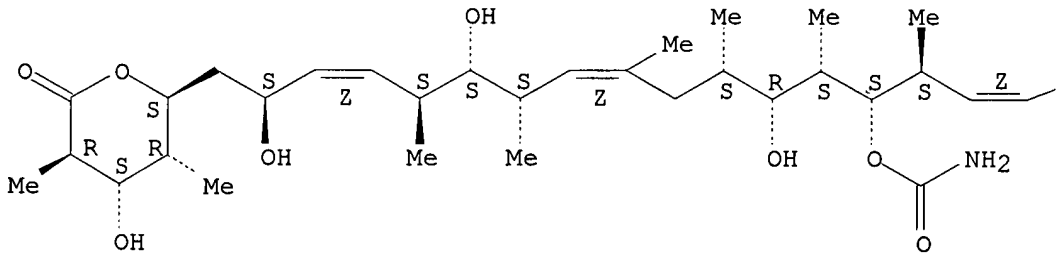
IT **127943-53-7DP**, Discodermolide, C(13)-C(21) fragment
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 127943-53-7 CAPLUS

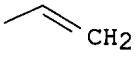
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



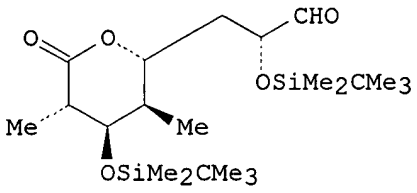
PAGE 1-B



L4 ANSWER 102 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:408992 CAPLUS
DOCUMENT NUMBER: 121:8992
TITLE: Studies towards the total synthesis of the

marine-derived immunosuppressant discodermolide; asymmetric synthesis of a C1-C8 .delta.-lactone subunit

AUTHOR(S): Paterson, Ian; Wren, Stephen P.
CORPORATE SOURCE: Univ. Chem. Lab., Cambridge, CB2 1EW, UK
SOURCE: Journal of the Chemical Society, Chemical Communications (1993), (24), 1790-2
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The C(1)-C(8) subunit I of discodermolide was prepd. in 9 steps and 41% overall yield and 97% overall diastereoselectivity from (R)-PhCH2OCH2CHMeCOEt via a stereoselective, boron-mediated, aldol-redn. sequence.

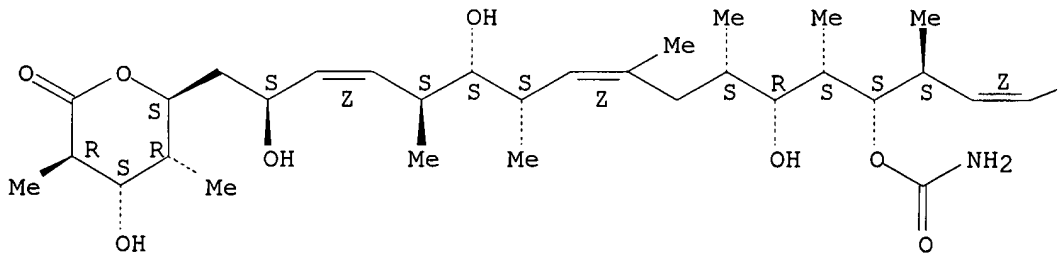
IT **127943-53-7P**, Discodermolide
RL: SPN (Synthetic preparation); PREP (Preparation)
(pyranpropanaldehyde fragment of, stereoselective prepn. of)

RN 127943-53-7 CAPLUS

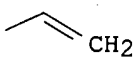
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



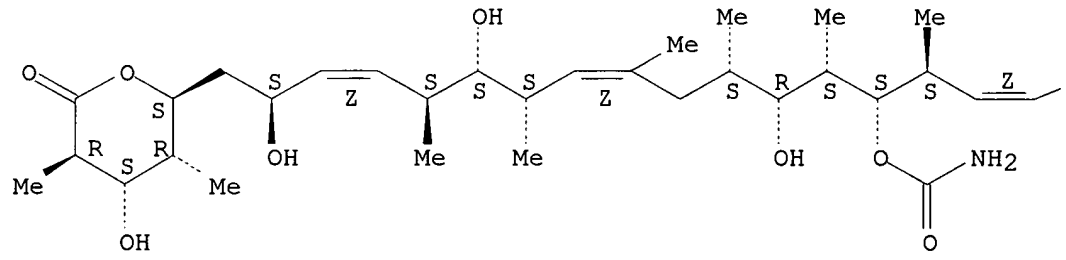
PAGE 1-B



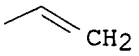
L4 ANSWER 103 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:260323 CAPLUS
DOCUMENT NUMBER: 120:260323
TITLE: Immunosuppression by discodermolide
AUTHOR(S): Longley, Ross E.; Gunasekera, Sarath P.; Faherty, Denise; McLane, John; Dumont, Francis
CORPORATE SOURCE: Div. Biomed. Mar. Res., Harbor Branch Oceanogr. Inst., Fort Pierce, FL, 34946, USA
SOURCE: Annals of the New York Academy of Sciences (1993), 696(Immunosuppressive and Antiinflammatory Drugs), 94-107
CODEN: ANYAA9; ISSN: 0077-8923
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 15 refs. on discodermolide's immunosuppressive activity and its ability to block proliferation in lymphoid and nonlymphoid cells.
IT **127943-53-7**, Discodermolide
RL: BIOL (Biological study)
(immunosuppression by)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

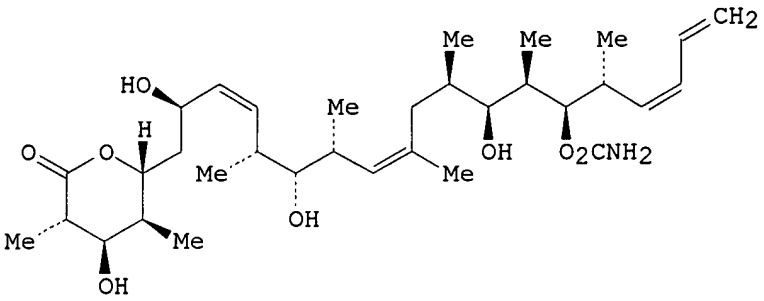


PAGE 1-B



L4 ANSWER 104 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:244430 CAPLUS
DOCUMENT NUMBER: 120:244430
TITLE: Total synthesis of the immunosuppressive agent (-)-discodermolide
AUTHOR(S): Nerenberg, Jennie B.; Hung, Deborah T.; Somers, Patricia K.; Schreiber, Stuart L.
CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA
SOURCE: Journal of the American Chemical Society (1993), 115(26), 12621-2
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The marine natural product discodermolide has been reported to inhibit the proliferation of lymphocytes. However, the inability to collect significant samples of the natural product from the sponge Discodermia dissoluta has prevented a detailed investigation of its mechanism of inhibition. The authors now report the first total synthesis of (-)-discodermolide (I) that proceeds in 36 total steps (longest linear sequence = 24 steps) and 3.2% overall yield. Three fragments that are prepd. by asym. crotyl addns. to a common aldehyde have been efficiently coupled by a Kishi-Nozaki type reaction with an iodoacetylene and a stereoselective alkylation reaction with a ketone enolate. I is a potent inhibitor of cell proliferation (no data).

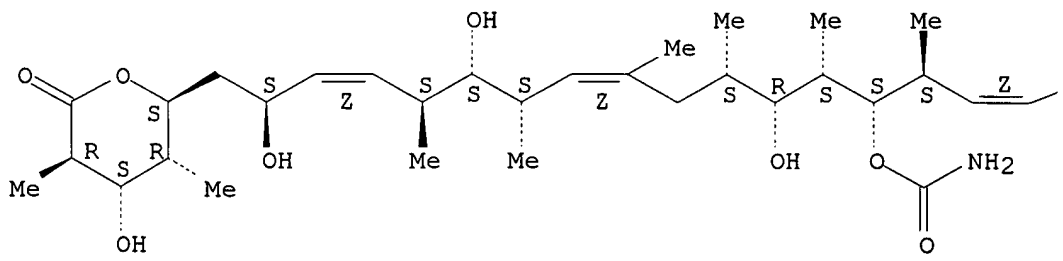
IT **127943-53-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(neoplasm-inhibiting activity)

RN 127943-53-7 CAPLUS

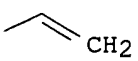
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



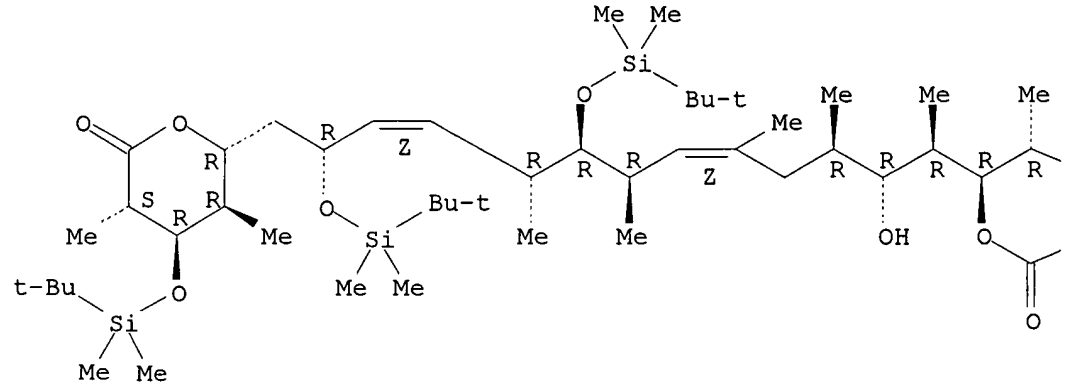
PAGE 1-B



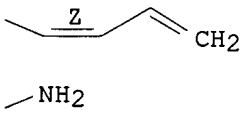
IT **153833-64-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 153833-64-8 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11S*,12S*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



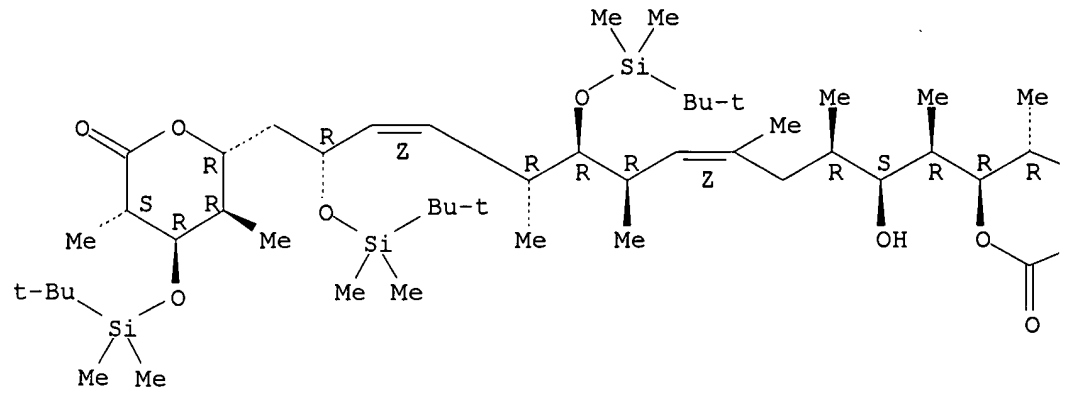
PAGE 1-B



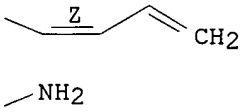
IT **153788-99-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate in total synthesis of discodermolide)
RN 153788-99-9 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6-bis[[(1,1-dimethylethyl)dimethylsilyl]oxy]-12-hydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-4-[[(1,1-dimethylethyl)dimethylsilyl]oxy]tetrahydro-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2S*,3Z,5S*,6S*,7S*,8Z,11S*,12R*,13S*,14S*,15S*,16Z)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



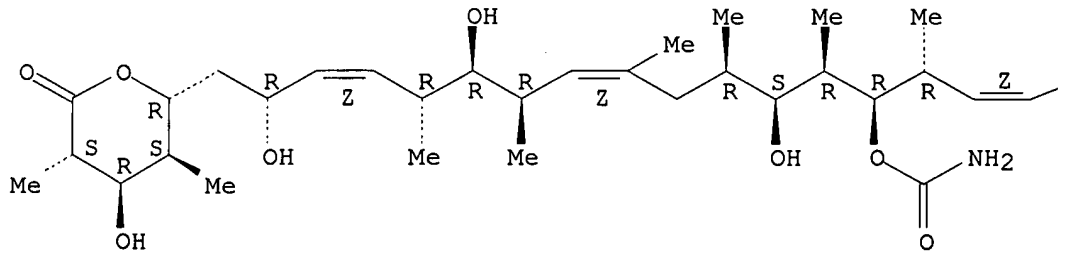
PAGE 1-B

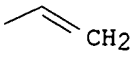


IT **154335-30-5P**, (-)-Discodermolide
RL: PREP (Preparation)
(total synthesis and neoplasm-inhibiting activity)
RN 154335-30-5 CAPLUS
CN 2H-Pyran-2-one, 6-[(2R,3Z,5R,6R,7R,8Z,11R,12S,13R,14R,15R,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3S,4R,5S,6R)- (9CI) (CA INDEX NAME)

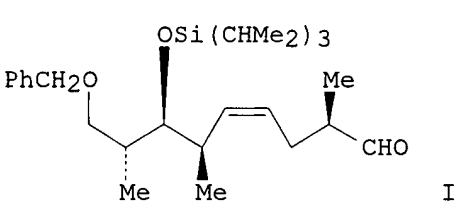
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

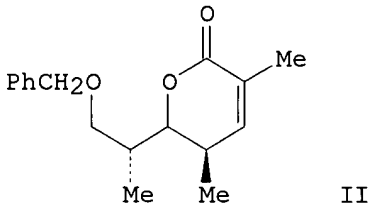




L4 ANSWER 105 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:218244 CAPLUS
DOCUMENT NUMBER: 120:218244
TITLE: The synthesis of a C(9)-C(17) fragment of discodermolide
AUTHOR(S): Evans, Phillip L.; Golec, Julian M. C.; Gillespie, Roger J.
CORPORATE SOURCE: Roussel Lab. Ltd., Covingham/Swindon/Wiltshire, SN3 5BZ, UK
SOURCE: Tetrahedron Letters (1993), 34(50), 8163-6
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:218244
GI



I



II

AB The asym. synthesis of synthetically useful fragment I corresponding to the C(9)-C(17) region of the immunosuppressant lactone discodermolide is reported. The route incorporates the use of unsatd. lactone II to provide a trisubstituted olefin with abs. control of geometry.

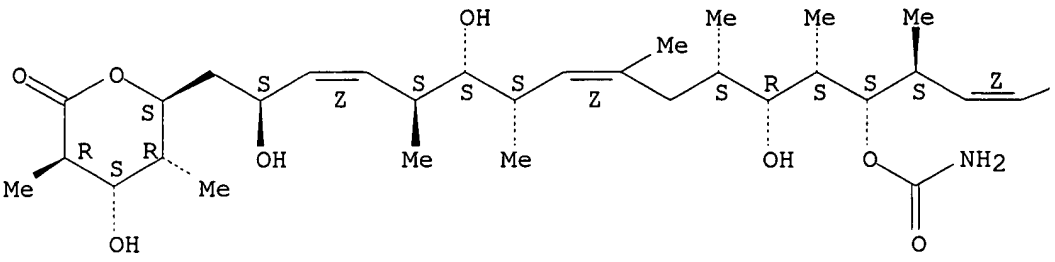
IT **127943-53-7P**, Discodermolide
RL: PREP (Preparation)
(synthesis of C(9)-C(17) fragment of)

RN 127943-53-7 CAPLUS

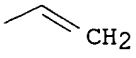
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

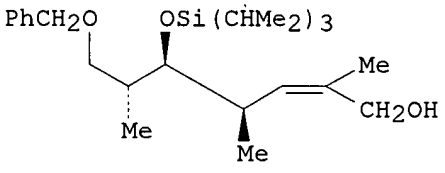


PAGE 1-B



L4 ANSWER 106 OF 111 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:192053 CAPLUS
DOCUMENT NUMBER: 120:192053
TITLE: An approach to the synthesis of a C(9)-C(15) fragment of discodermolide
AUTHOR(S): Golec, Julian M. C.; Gillespie, Roger J.
CORPORATE SOURCE: Roussel Lab. Ltd., Convingham/Swindon/Wiltshire, SN3 5BZ, UK
SOURCE: Tetrahedron Letters (1993), 34(50), 8167-8
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:192053
GI



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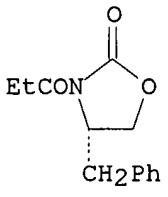


II

AB The asym. synthesis of synthetically useful fragment I corresponding to the C(9)-C(15) region of the immunosuppressant lactone discodermolide from oxazolidinone II is reported.

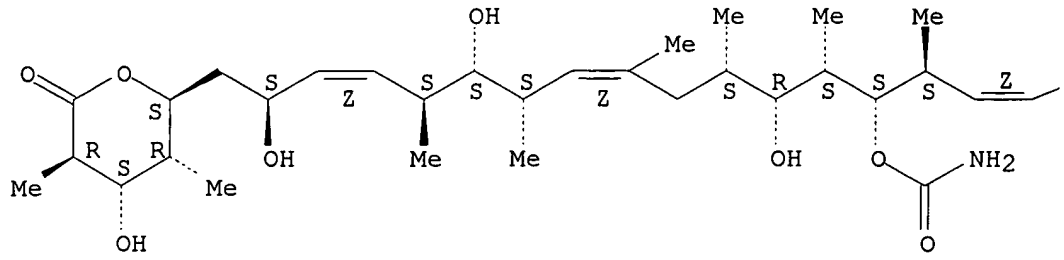
IT **127943-53-7P**, Discodermolide
RL: PREP (Preparation)
(approach to synthesis of C(9)-C(15) fragment of)

RN 127943-53-7 CAPLUS

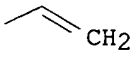
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

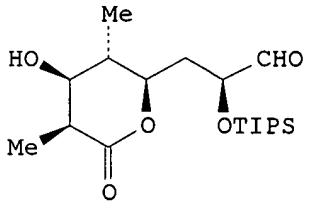
PAGE 1-A



PAGE 1-B



L4 ANSWER 107 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:164570 CAPLUS
DOCUMENT NUMBER: 120:164570
TITLE: The synthesis of a C1-C8 lactone fragment of discodermolide
AUTHOR(S): Golec, Julian M. C.; Jones, Stuart D.
CORPORATE SOURCE: Roussel Lab. Ltd., Covingham/Swindon/Wiltshire, SN3 5BZ, UK
SOURCE: Tetrahedron Letters (1993), 34(50), 8159-62
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 120:164570
GI



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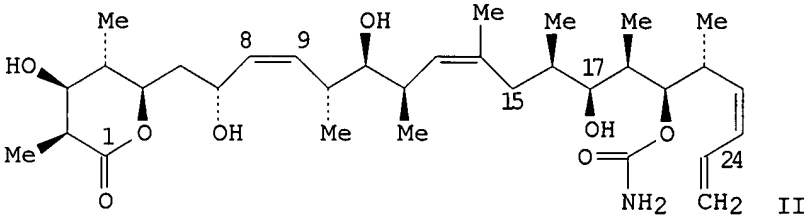
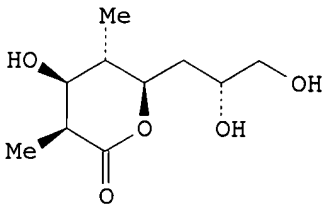


II



III

AB The asym. synthesis of fragment I corresponding to the C1-C8 region of the immunosuppressant discodermolide (II) is reported. Trihydroxylactone III of defined abs. stereochem. is also prepd. This compd. is a potential reductive ozonolysis product of II and may aid the detn. of the abs. stereochem. of the natural product.

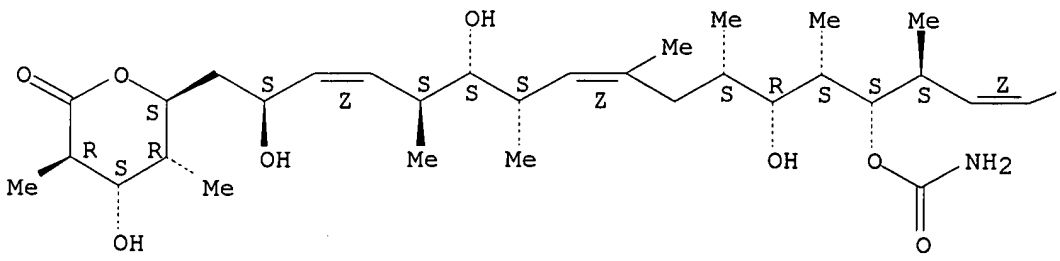
IT **127943-53-7**, Discodermolide
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthetic approach to lactone contg. fragment of)

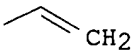
RN 127943-53-7 CAPLUS

CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

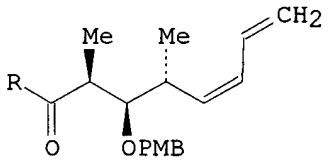
Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A





L4 ANSWER 108 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:670898 CAPLUS
DOCUMENT NUMBER: 119:270898
TITLE: Studies on the alkylation of chiral enolates: application toward the total synthesis of discodermolide
AUTHOR(S): Clark, David L.; Heathcock, Clayton H.
CORPORATE SOURCE: Dep. Chem., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Journal of Organic Chemistry (1993), 58(22), 5878-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:270898
GI



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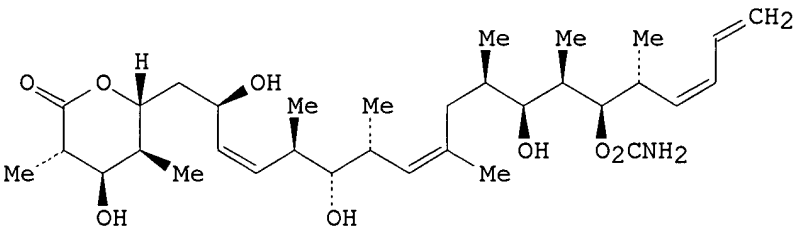

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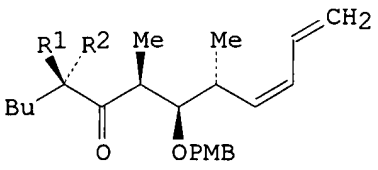


III

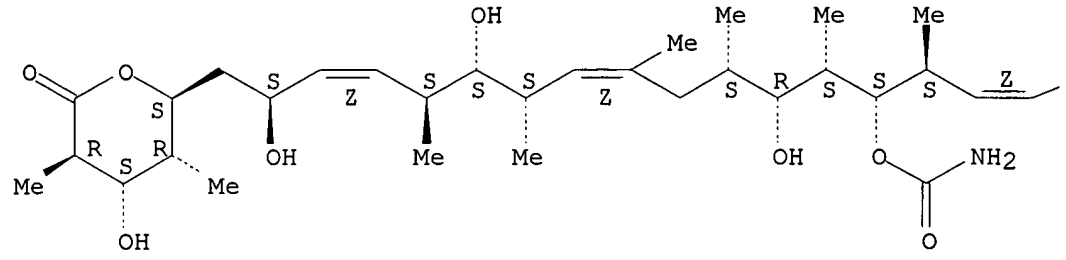
AB The alkylation of the lithium Z enolates derived from ketones I (R = Et, pentyl) has been studied as a model for the synthesis of the potent immunosuppressive agent discodermolide (II). Alkylation of I (R = Et) with BuI gave ketone III (R1 = H, R2 = Me), whereas alkylation of I (R = pentyl) with MeI provided III (R1 = Me, R2 = H). These results suggest that internal .beta.-chelation of the enolate is not involved as a stereochem. control element.

IT **127943-53-7**, Discodermolide

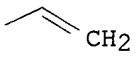
RL: RCT (Reactant); RACT (Reactant or reagent)
(C(16)-C(24) fragment of, model for)
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

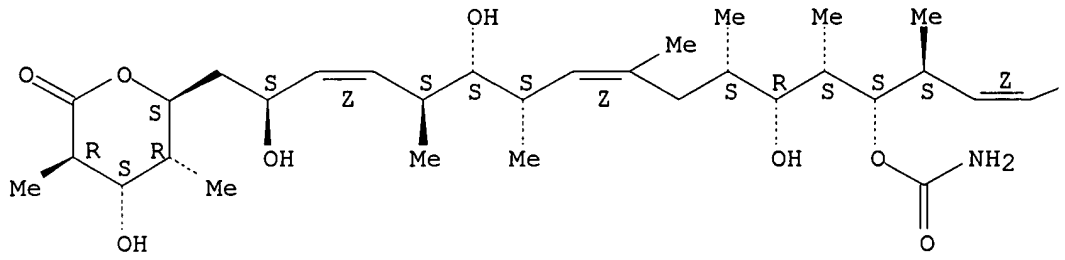


L4 ANSWER 109 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:244552 CAPLUS
DOCUMENT NUMBER: 114:244552
TITLE: Discodermolide: a new bioactive polyhydroxylated lactone from the marine sponge Discodermia dissoluta [Erratum to document cited in CA113(9):75187b]
AUTHOR(S): Gunasekera, Sarath P.; Gunasekera, Malika; Longley, Ross E.; Schulte, Gayle K.
CORPORATE SOURCE: Div. Biomed. Mar. Res., Harbor Branch Oceanogr. Inst., Inc., Ft. Pierce, FL, 34946, USA
SOURCE: Journal of Organic Chemistry (1991), 56(3), 1346
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Errors in the stereochem. of structures 1 and 2 have been cor. The error was reflected in the index entries.
IT **127943-53-7**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of sponge, isolation and mol. structure and biol. activity of (Erratum))
RN 127943-53-7 CAPLUS
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

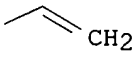
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



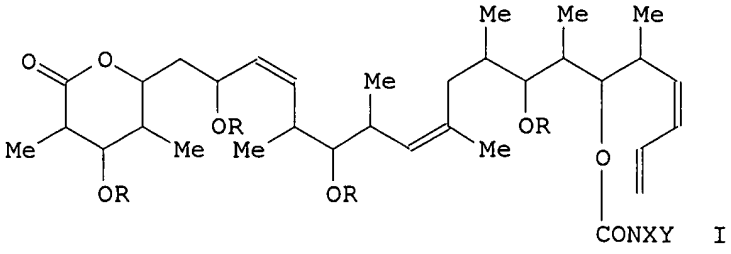
PAGE 1-B



L4 ANSWER 110 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:631094 CAPLUS
DOCUMENT NUMBER: 113:231094
TITLE: Preparation of discodermolide compounds as antitumor agents and immunosuppressants
INVENTOR(S): Gunasekera, Malika; Gunasekera, Sarath P.; Longley, Ross E.; Burres, Neal S.
PATENT ASSIGNEE(S): Harbor Branch Oceanographics Institution, Inc., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4939168	A	19900703	US 1989-392468	19890811
US 5010099	A	19910423	US 1990-519605	19900507
CA 2056412	AA	19910212	CA 1990-2056412	19900809
WO 9101982	A1	19910221	WO 1990-US4493	19900809
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
EP 486565	A1	19920527	EP 1990-912243	19900809
EP 486565	B1	19950426		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04507245	T2	19921217	JP 1990-511555	19900809
JP 3008985	B2	20000214		
AT 121739	E	19950515	AT 1990-912243	19900809
ES 2071826	T3	19950701	ES 1990-912243	19900809

PRIORITY APPLN. INFO.: US 1989-392468 A3 19890811
WO 1990-US4493 W 19900809
OTHER SOURCE(S): MARPAT 113:231094
GI



I

AB Title compds. I (R = H, alkyl, CH2, Ph, tolyl, xylyl, alkylcarbonyl, ZCO, Z = (substituted) Ph; X = H, alkyl, Z, CH2Z; Y = H, alkyl, Z, CH2Z, alkylcarbonyl, ZCO) and salts thereof are prepd. The sponge Discodermia dissoluta was homogenized with MeOH-H2O to give an impure discodermolide I (R = X = Y = H) (II), which was subjected to HPLC to give pure II. II was immunosuppressive in murine mixed lymphocyte reaction at 0.5 .mu.g/mL and at 20 .mu.g/mL showed 92% inhibited the proliferation of cultured murine P398 cells.

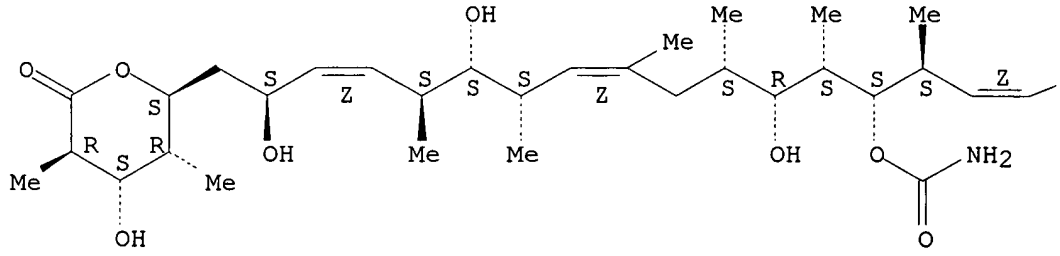
IT **127943-53-7P 130604-09-0P 130604-10-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as antitumor agent and immunosuppressant)

RN 127943-53-7 CAPLUS

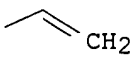
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



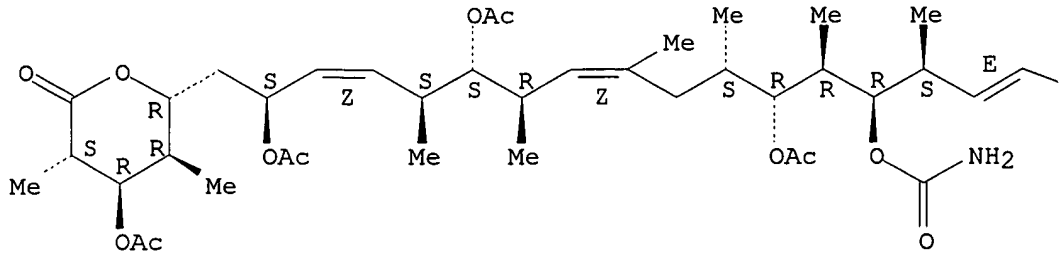
RN 130604-09-0 CAPLUS

CN 2H-Pyran-2-one, 4-(acetyloxy)tetrahydro-3,5-dimethyl-6-[2,6,12-tris(acetyloxy)-14-[(aminocarbonyl)oxy]-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2R*,3Z,5R*,6R*,7S*,8Z,11R*,12S*,13S*,14S*,15R*,16E)]]- (9CI) (CA INDEX NAME)

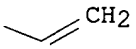
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



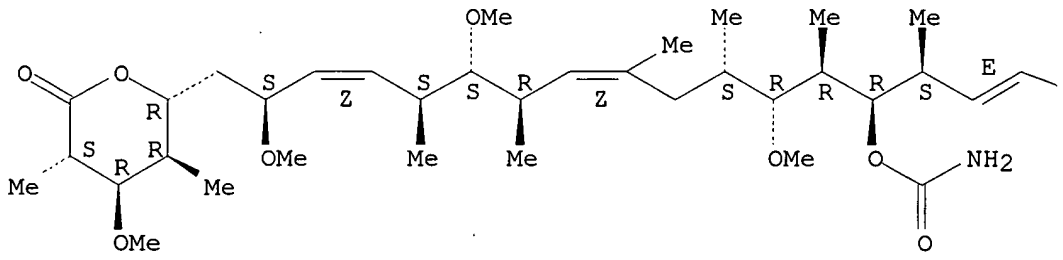
PAGE 1-B



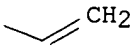
RN 130604-10-3 CAPLUS
CN 2H-Pyran-2-one, 6-[14-[(aminocarbonyl)oxy]-2,6,12-trimethoxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-methoxy-3,5-dimethyl-, [3S-[3.alpha.,4.beta.,5.beta.,6.alpha.(2R*,3Z,5R*,6R*,7S*,8Z,11R*,12S*,13S*,14S*,15R*,16E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

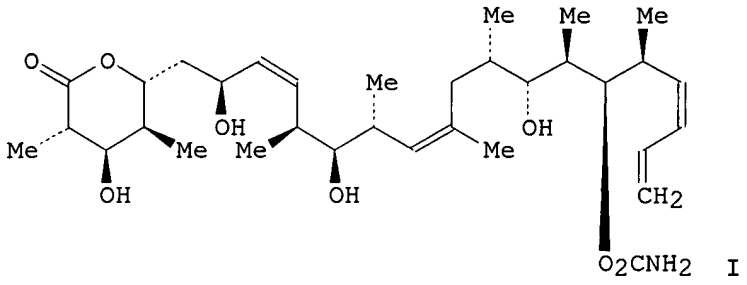


PAGE 1-B



L4 ANSWER 111 OF 111 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1990:475187 CAPLUS
DOCUMENT NUMBER: 113:75187
TITLE: Discodermolide: a new bioactive polyhydroxylated lactone from the marine sponge Discodermia dissoluta
AUTHOR(S): Gunasekera, Sarath P.; Gunasekera, Malika; Longley, Ross E.; Schulte, Gayle K.
CORPORATE SOURCE: Div. Biomed. Mar. Res., Harbor Branch Oceanogr. Inst., Inc., Ft. Pierce, FL, 34946, USA

SOURCE: Journal of Organic Chemistry (1990), 55(16), 4912-15
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A new polyhydroxylated lactone, discodermolide (I) was isolated from a Caribbean marine sponge, D. dissoluta, and its structure was elucidated through a combination of spectroscopic techniques, in particular NMR spectroscopy, and verified by x-ray crystallog. anal. The C skeleton displayed by discodermolide is new; disodermolide is immunosuppressive and cytotoxic.

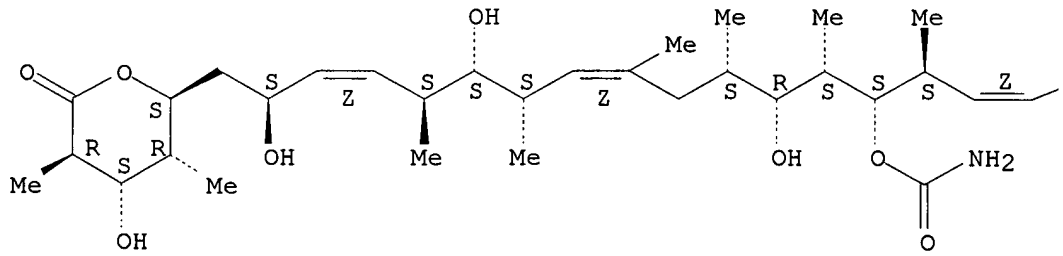
IT **127943-53-7**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(of sponge, isolation and mol. structure and biol. activity of)

RN 127943-53-7 CAPLUS

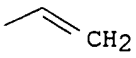
CN 2H-Pyran-2-one, 6-[(2S,3Z,5S,6S,7S,8Z,11S,12R,13S,14S,15S,16Z)-14-[(aminocarbonyl)oxy]-2,6,12-trihydroxy-5,7,9,11,13,15-hexamethyl-3,8,16,18-nonadecatetraenyl]tetrahydro-4-hydroxy-3,5-dimethyl-, (3R,4S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



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L2 8 S L1
L3 178 S L1 FULL

FILE 'CAPLUS' ENTERED AT 16:27:28 ON 06 NOV 2002
L4 111 S L3

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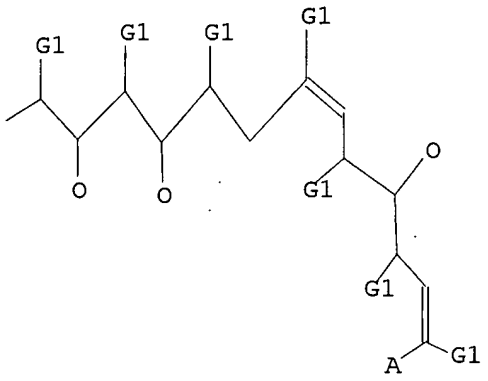
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak

Structure attributes must be viewed using STN Express query preparation.

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Executing the logoff script...

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	475.14	616.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-61.33	-61.33

STN INTERNATIONAL LOGOFF AT 16:33:16 ON 06 NOV 2002